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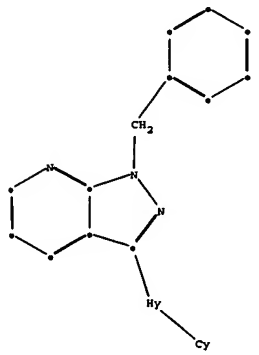

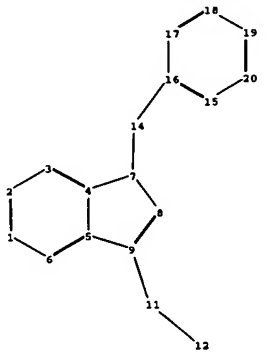

chain nodes :
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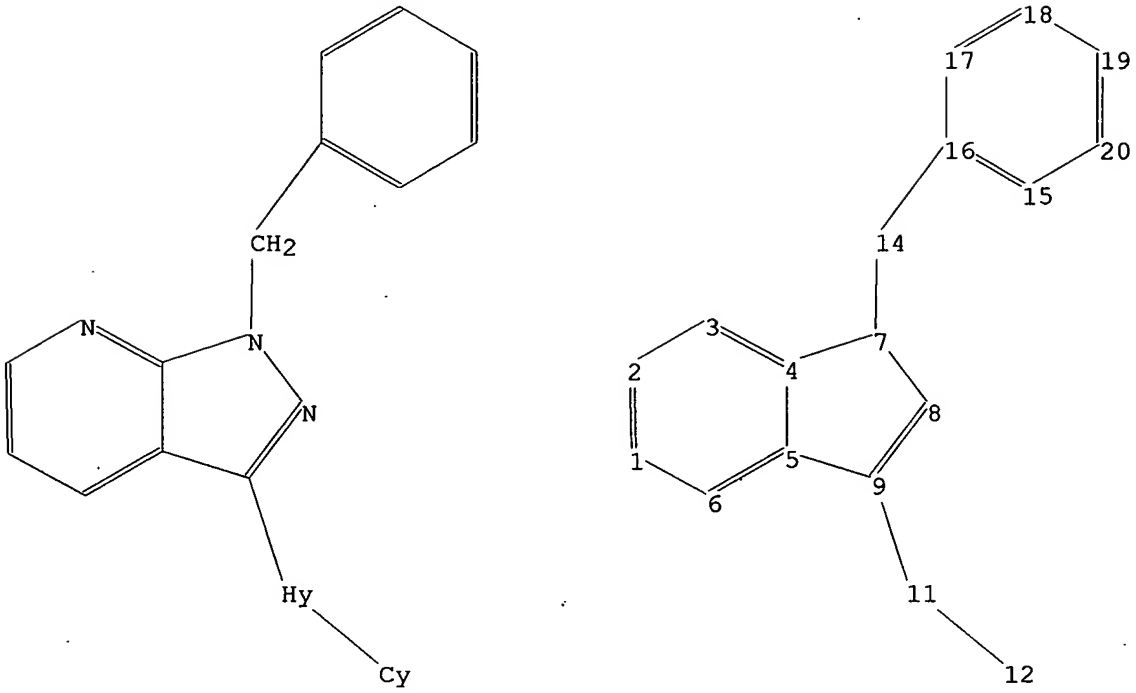
ring nodes :
    1 2 3 4 5 6 7 8 9 15 16 17 18 19 20
chain bonds :
    7-14 9-11 11-12 14-16
ring bonds :
    1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 15-16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
    4-7 7-8 8-9 9-11 11-12
exact bonds :
    5-9 7-14 14-16
normalized bonds :
    1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
isolated ring systems :
    containing 1 : 15 :

Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:Atom 12:Atom
    14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
Generic attributes :
    11:
    Saturation   : Unsaturated
    Number of Carbon Atoms : less than 7
    Number of Hetero Atoms : 2 or more
    Type of Ring System   : Monocyclic

Element Count :
    Node 11: Limited
        C,C4
        N,N2

O,OO
S,SO

=>
Uploading C:\Program Files\Stnexp\Queries\10521538.str



chain nodes :
11 12 14
ring nodes :
1 2 3 4 5 6 7 8 9 15 16 17 18 19 20
chain bonds :
7-14 9-11 11-12 14-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 15-16 15-20 16-17 17-18 18-19
19-20
exact/norm bonds :
4-7 7-8 8-9 9-11 11-12
exact bonds :
5-9 7-14 14-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
isolated ring systems :
containing 1 : 15 :

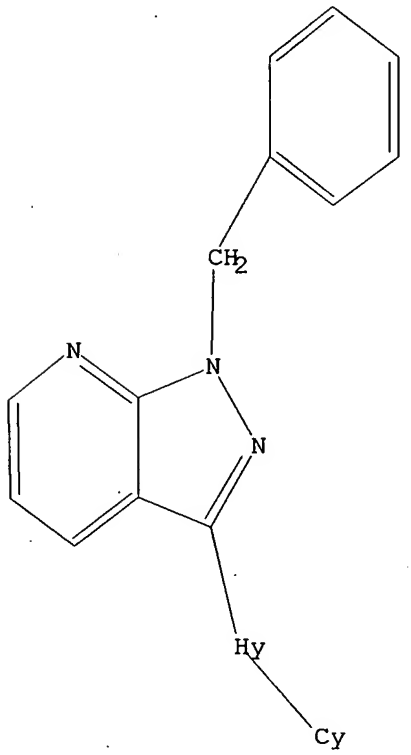
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:Atom
12:Atom 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
Generic attributes :
11:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : 2 or more
Type of Ring System : Monocyclic

Element Count :

Node l1: Limited
C,C4
N,N2
O,O0
S,S0

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 12:19:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 115 TO ITERATE

100.0% PROCESSED 115 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1657 TO 2943

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PROJECTED ANSWERS:                6 TO      266

L2             6 SEA SSS SAM L1

=> => s l1 sss ful
FULL SEARCH INITIATED 12:20:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     1929 TO ITERATE

100.0% PROCESSED     1929 ITERATIONS                          131 ANSWERS
SEARCH TIME: 00.00.01

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=> => s l3
L4           60 L3

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L4 ANSWER 1 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:902719 CAPLUS
DN 143:235464
TI Enhancing the effectiveness of an inhaled therapeutic gas
IN Bloch, Kenneth D.; Ichinose, Fumito; Zapol, Warren M.; Evgenov, Oleg V.
PA The General Hospital Corporation, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005077005	A2	20050825	WO 2005-US3877	20050204

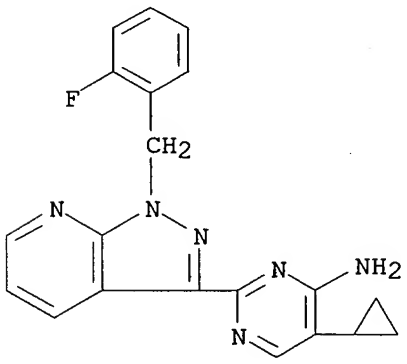
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-542000P P 20040204

AB Methods for enhancing the therapeutic or prophylactic effectiveness of an inhaled therapeutic gas include administering to a mammal by inhalation a therapeutically effective amount of gaseous nitric oxide or carbon monoxide, and administering to the mammal a composition containing a compound that sensitizes soluble guanylate cyclase. Pharmacol. sensitization of soluble guanylate cyclase with Bay 41-2272 produced pulmonary vasodilation and modulation of pulmonary response to inhaled nitric oxide.

IT **256376-24-6**, Bay 41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancing the effectiveness of an inhaled therapeutic gas)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

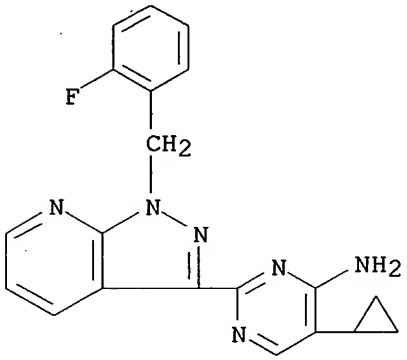


L4 ANSWER 2 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:624333 CAPLUS
DN 143:227271
TI Stimulation of soluble guanylate cyclase slows progression in anti-thy1-induced chronic glomerulosclerosis
AU Wang, Yingrui; Kraemer, Stephanie; Loof, Tanja; Martini, Sebastian; Kron, Susanne; Kawachi, Hiroshi; Shimizu, Fuijo; Neumayer, Hans-H.; Peters, Harm
CS Department of Nephrology and Center of Cardiovascular Research, Charite University Medicine Berlin, Humboldt University, Berlin, Germany
SO Kidney International (2005), 68(1), 47-61
CODEN: KDYIA5; ISSN: 0085-2538
PB Blackwell Publishing, Inc.
DT Journal
LA English
AB Background: A critical role of soluble guanylate cyclase and nitric oxide-dependent cyclic 3',5'-guanosine monophosphate (cGMP) production for glomerular matrix expansion has recently been documented in a rat model of acute anti-thy1 glomerulonephritis. The present study analyzes the renal activity of the nitric oxide-cGMP signaling cascade in and the effect of the specific soluble guanylate cyclase stimulator Bay 41-2272 on a progressive model of anti-thy1-induced chronic glomerulosclerosis. Methods: Anti-thy1 glomerulosclerosis was induced by injection of anti-thy1 antibody into uninephrectomized rats. One week after disease induction, animals were randomly assigned to chronic glomerulosclerosis, chronic glomerulosclerosis plus Bay 41-2272 (10 mg/kg body weight/day) or chronic glomerulosclerosis plus hydralazine (15 mg/kg body weight/day). In week 16, anal. included effects on systolic blood pressure, proteinuria, kidney function, glomerular and tubulointerstitial matrix protein accumulation, expression of transforming growth factor-β1 (TGF-β1), fibronectin and plasminogen activator inhibitor type 1 (PAI-1), macrophage infiltration, cell proliferation, basal and nitric oxide-stimulated cGMP production as well as tubulointerstitial mRNA expression of alpha 1 and beta 1 soluble guanylate cyclase. Results: The moderately elevated systolic blood pressure seen in the chronic glomerulosclerosis group was comparably decreased by both treatments. Compared to normal controls, soluble guanylate cyclase mRNA expression and nitric oxide-stimulated cGMP production were up-regulated in the tubulointerstitium of the untreated chronic glomerulosclerosis animals, while its activity was decreased in glomeruli. Bay 41-2272 treatment enhanced glomerular and tubulointerstitial nitric oxide-cGMP signaling significantly. This went along with markedly reduced glomerular and tubulointerstitial macrophage infiltration, number of proliferating cells, matrix expression and accumulation, as well as improved kidney function. In contrast, hydralazine therapy did not significantly affect renal nitric oxide-cGMP signaling, macrophage number, cell proliferation, matrix protein expression and accumulation. Conclusion: Glomerular and tubulointerstitial soluble guanylate cyclase activity are discordantly altered in anti-thy1-induced chronic glomerulosclerosis. Stimulation of soluble guanylate cyclase signaling by Bay 41-2272 limits the progressive course of this model toward tubulointerstitial fibrosis and impaired renal function at least in part in a blood pressure-independent manner. The results suggest that soluble guanylate cyclase activation counteracts fibrosis and progression in chronic renal disease.
IT **256376-24-6**, Bay 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stimulation of soluble guanylate cyclase by Bay 41-2272 enhanced nitric oxide-cGMP signaling and improved renal function limiting progression towards tubulointerstitial fibrosis in rat model of anti-thy1-induced

chronic glomerulosclerosis)

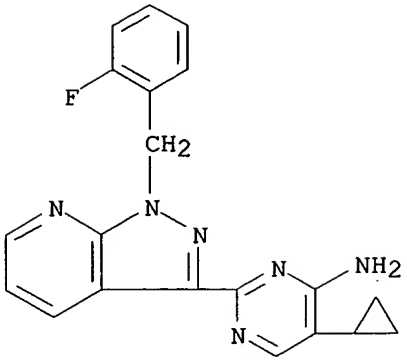
RN 256376-24-6 CAPLUS

CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:603087 CAPLUS
DN 143:146287
TI BAY 41-2272 [5-cyclopropyl-2-[1-(2-fluoro-benzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]pyrimidin-4-ylamine]-induced dilation in ovine pulmonary artery: Role of sodium pump
AU Bawankule, Dnyaneshwar U.; Sathishkumar, K.; Sardar, Kautuk K.; Chanda, Debabrata; Krishna, A. Vamsi; Prakash, Vellanki Ravi; Mishra, Santosh K.
CS Division of Pharmacology and Toxicology, Indian Veterinary Research Institute, India
SO Journal of Pharmacology and Experimental Therapeutics (2005), 314(1), 207-213
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The mechanisms of relaxation to nitric oxide (NO)-independent soluble guanylyl cyclase (sGC) activator BAY 41-2272 were investigated in isolated ovine pulmonary artery. BAY 41-2272 (1 nM-10 μM) produced concentration-dependent relaxation of endothelium-denuded pulmonary artery rings (pD2 = 6.82±0.16; Emax = 92.30±2.31%; n = 8), precontracted with 1 μM 5-hydroxytryptamine (serotonin). 1-H-[1,2,4]Oxadiazole[4,3-a]quinoxalin-1-one (ODQ; 10 μM), an inhibitor of sGC, partially inhibited (Emax = 57.10±3.10%; n = 6) the relaxation response of BAY 41-2272. In comparison with ODQ, sodium pump inhibitor ouabain (1 μM) produced a greater decrease in the vasodilator response of BAY 41-2272 (Emax = 20.17±4.55%; n = 6). K+-free solution also attenuated (Emax = 39.97±3.52%; n = 6) BAY 41-2272-induced relaxation. ODQ (10 μM) plus 1 μM ouabain abolished the relaxant response of BAY 41-2272 (Emax = 12.09±3.76%, n = 6 vs. vehicle control DMSO; Emax = 15.83±1.72%, n = 6). KT-5823 (2 μM), a specific inhibitor of protein kinase G had no effect on 10 μM ODQ-insensitive relaxation evoked by BAY 41-2272. BAY 41-2272 (10 μM) inhibited Ca2+-induced contractions in K+-depolarized prepns. BAY 41-2272 (10 μM) caused about a 14-fold increase in the intracellular cGMP over the basal level, which was completely inhibited by 10 μM ODQ. BAY 41-2272 (0.1, 1.0, and 10 μM) significantly ($P < 0.05$) increased ouabain-sensitive 86Rb uptake in a concentration-dependent manner. BAY 41-2272 (10 μM) also stimulated sarcolemmal Na+-K+-ATPase activity. However, 10 μM ODQ had no significant effect on either basal or BAY 41-2272-stimulated 86Rb uptake/Na+-K+-ATPase activities. In conclusion, this study provides the first evidence of sodium pump stimulation by BAY 41-2272 independent of cGMP as an addnl. mechanism to sGC activation in relaxation of ovine pulmonary artery.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); BIOL (Biological study)
(BAY 41-2272-induced dilation in ovine pulmonary artery: role of sodium pump)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:451176 CAPLUS
DN 143:1222
TI Modulating substances of the nitric oxide-cyclic guanosine 3',5'-monophosphate signaling pathway for the treatment of dental disorders
IN Baumann, Michael; Bloch, Wilhelm; Korkmaz, Yueksel
PA Cell Center Cologne G.m.b.H., Germany
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

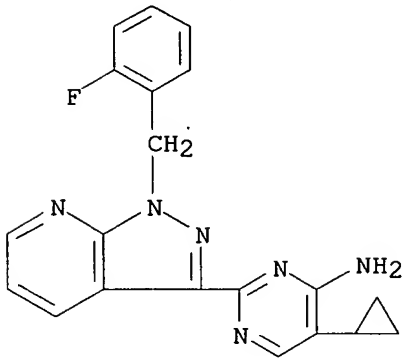
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005046660	A1	20050526	WO 2004-EP12935	20041115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-26132 A 20031113

AB The use of a modulating substance of the nitric oxide (NO)-cyclic guanosine 3',5'-monophosphate (cGMP) signaling pathway for the preparation of a pharmaceutical composition for the prevention and/or treatment of a dental disorder in a mammal is disclosed. Furthermore, pharmaceutical compns. comprising a modulating substance of the NO-cGMP signaling pathway as well as methods for treating a dental disorder are provided.

IT **256376-24-6**, BAY 41-2272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulating substances of the nitric oxide-cyclic GMP signaling pathway for the treatment of dental disorders)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:409351 CAPLUS
DN 142:435861
TI Novel combination for treating hypertension
IN Fox, David Nathan Abraham; Karran, Eric
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005042022	A2	20050512	WO 2004-IB3444	20041020
WO 2005042022	A3	20050804		

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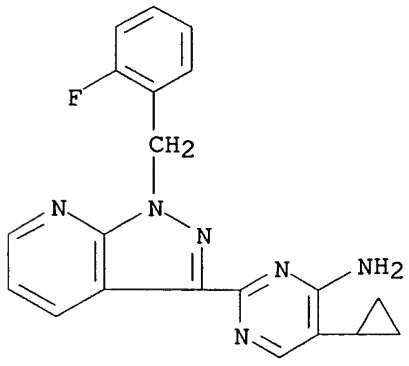
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2003-25291 A 20031029

AB Combination comprising (a) an activator of soluble guanylate cyclase and (b) and angiotensin II receptor antagonist are useful for treating hypertension. Active ingredients (50 mg) were blended with cellulose (microcryst.), silicon dioxide, stearic acid (fumed), and the mixture was compressed to form tablets.

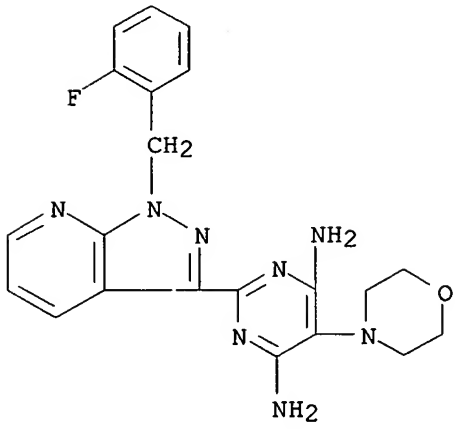
IT **256376-24-6**, BAY41-2272 **256498-66-5**, BAY41-8543
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel combination for treating hypertension)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

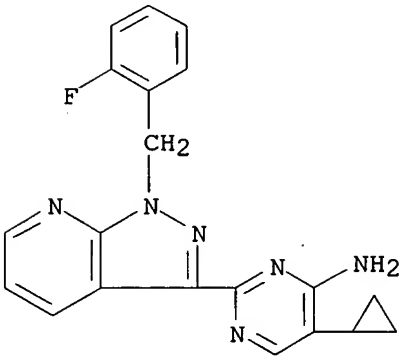


RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-

b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

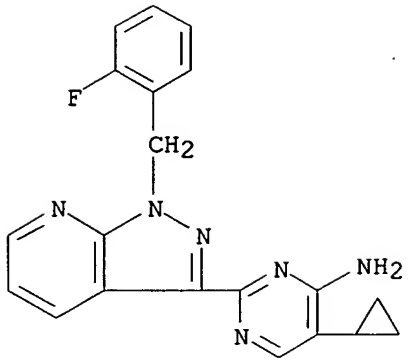


L4 ANSWER 6 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:387239 CAPLUS
DN 143:92904
TI Residues stabilizing the heme moiety of the nitric oxide sensor soluble guanylate cyclase
AU Schmidt, Peter M.; Rothkegel, Christiane; Wunder, Frank; Schroeder, Henning; Stasch, Johannes-Peter
CS Institute of Cardiovascular Research, Bayer Healthcare, Wuppertal, D-42096, Germany
SO European Journal of Pharmacology (2005), 513(1-2), 67-74
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier B.V.
DT Journal
LA English
AB Soluble guanylate cyclase, a heterodimer consisting of an α- and a heme-containing β-subunit, is the major receptor for the biol. messenger nitric oxide (NO) and is involved in various signal transduction pathways. The heme moiety of the enzyme is bound between the axial heme ligand histidine105 and the recently identified counterparts of the heme propionic acids, tyrosine135 and arginine139. The latter residues together with an invariant serine137 form the unique heme binding motif Y-x-S-x-R. In this work, we show that replacement of the serine137 with alanine destabilizes the binding of the heme moiety and impairs NO-mediated soluble guanylate cyclase activation.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S137A mutant residue of soluble guanylate cyclase plays role in destabilizing binding of heme moiety and impairs NO-mediated soluble guanylate cyclase activation)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



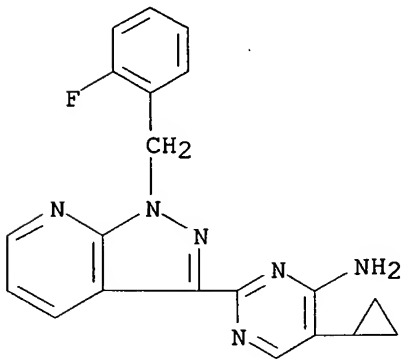
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:338069 CAPLUS
DN 142:456681
TI Effects of BAY 41-2272, a soluble guanylate cyclase activator, on pulmonary vascular reactivity in the ovine fetus
AU Deruelle, Philippe; Grover, Theresa R.; Storme, Laurent; Abman, Steven H.
CS Pediatric Heart Lung Center, University of Colorado School of Medicine, Denver, CO, USA
SO American Journal of Physiology (2005), 288(4, Pt. 1), L727-L733
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Nitric oxide (NO)-cGMP signaling plays a critical role during the transition of the pulmonary circulation at birth. BAY 41-2272 is a novel NO-independent direct stimulator of soluble guanylate cyclase that causes vasodilation in systemic and local circulations. However, the hemodynamic effects of BAY 41-2272 have not been studied in the perinatal pulmonary circulation. We hypothesized that BAY 41-2272 causes potent and sustained fetal pulmonary vasodilation. We performed surgery on 14 fetal lambs (125-130 days gestation; term = 147 days) and placed catheters in the main pulmonary artery, aorta, and left atrium to measure pressures. An ultrasonic flow transducer was placed on the left pulmonary artery (LPA) to measure blood flow, and a catheter was placed in the LPA for drug infusion. Pulmonary vascular resistance (PVR) was calculated as pulmonary artery pressure minus left atrial pressure divided by LPA blood flow. BAY 41-2272 caused dose-related increases in pulmonary blood flow up to threefold above baseline and reduced PVR by 75% ($P < 0.01$). Prolonged infusion of BAY 41-2272 caused sustained pulmonary vasodilation throughout the 120-min infusion period. The pulmonary vasodilator effect of BAY 41-2272 was not attenuated by Nω-nitro-L-arginine, a NO synthase inhibitor. In addition, compared with sildenafil, a phosphodiesterase 5 inhibitor, the pulmonary vasodilator response to BAY 41-2272 was more prolonged. We conclude that BAY 41-2272 causes potent and sustained fetal pulmonary vasodilation independent of NO release. We speculate that BAY 41-2272 may have therapeutic potential for pulmonary hypertension associated with failure to circulatory adaptation at birth, especially in the setting of impaired NO production
IT **256376-24-6**, BAY 41-2272
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of BAY 41-2272, a soluble guanylate cyclase activator, on pulmonary vascular reactivity in ovine fetus)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:337952 CAPLUS
DN 142:423474
TI Stimulation of soluble guanylyl cyclase inhibits mesangial cell proliferation and matrix accumulation in experimental glomerulonephritis
AU Hohenstein, Bernd; Daniel, Christoph; Wagner, Andrea; Stasch, Johannes-Peter; Hugo, Christian
CS Department of Nephrology, University of Erlangen-Nuremberg, Erlangen, Germany
SO American Journal of Physiology (2005), 288(4, Pt. 2), F685-F693
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB To date, no specific treatment is established in mesangial proliferative glomerulonephritis in humans. Specific stimulation of soluble guanylyl cyclase (sGC), an enzyme catalyzing the synthesis of cGMP from GTP, can be achieved by the novel pyrazolopyridine derivative BAY 41-2272. The effect of sGC stimulation via BAY 41-2272 on mesangial proliferation was assessed in vivo using a mesangial proliferative glomerulonephritis model in rats (anti-Thy1 model). Renal biopsies, as well as glomerular isolates, urine samples, and blood samples were compared in BAY 41-2272- and placebo-treated groups during anti-Thy1 nephritis. The sGC β1-subunit is upregulated during anti-Thy1 nephritis and mainly confined to mesangial areas by immunohistochem. Specific therapeutic sGC stimulation during anti-Thy1 nephritis in vivo was achieved via BAY 41-2272 treatment as demonstrated by increased glomerular cGMP levels causing inhibition of mesangial proliferation, glomerular matrix accumulation, and proteinuria compared with placebo-treated animals. SGC is tightly regulated in glomeruli during exptl. glomerulonephritis. Considering its beneficial antiproliferative, antifibrotic, and antiproteinuric effect in exptl. glomerulonephritis, the therapeutic stimulation of sGC could become a promising future goal in mesangial proliferative glomerulonephritis in humans.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stimulation of soluble guanylyl cyclase inhibits mesangial cell proliferation and matrix accumulation in exptl. glomerulonephritis)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



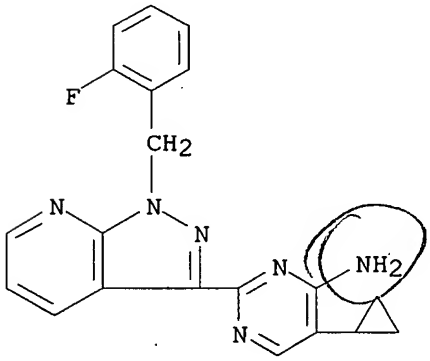
L4 ANSWER 9 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:259829 CAPLUS
DN 142:329823
TI Potassium channel mediated delivery of agents through the blood-brain barrier
IN Black, Keith L.; Ningaraj, Nagendra S.
PA Cedars-Sinai Medical Center, USA
SO PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005025511	A2	20050324	WO 2004-US29787	20040910
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005089473	A1	20050428	US 2004-938674	20040910
PRAI	US 2003-502159P	P	20030910		
	US 2003-528440P	P	20031210		
	US 2004-548636P	P	20040227		

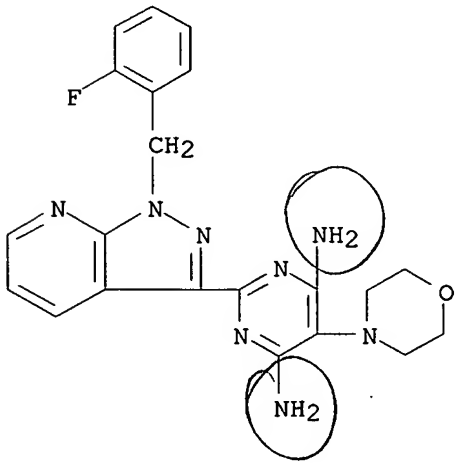
AB This invention includes pharmaceutical compns., methods and. kits for the treatment or diagnosis of a malignant tumors, including brain tumors, and diseases or disorders characterized by abnormal brain tissue.

IT **256376-24-6**, BAY 41-2272 **256498-66-5**, BAY 41-8543
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potassium channel mediated delivery of agents through the blood-brain barrier)

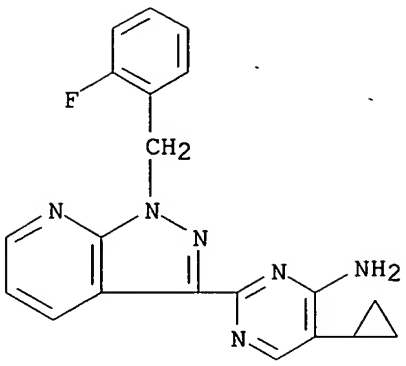
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

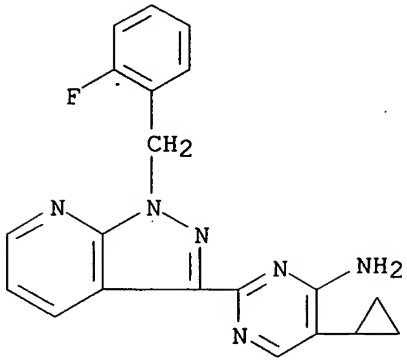


L4 ANSWER 10 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:208470 CAPLUS
DN 142:443670
TI Resonance Raman and Infrared Spectroscopic Studies of High-Output Forms of Human Soluble Guanylyl Cyclase
AU Martin, Emil; Czarnecki, Kazimierz; Jayaraman, Vasanthi; Murad, Ferid; Kincaid, James
CS Department of Integrative Biology and Institute of Molecular Medicine, University of Texas Houston Medical School, Houston, TX, 77030, USA
SO Journal of the American Chemical Society (2005), 127(13), 4625-4631
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The allosteric regulator BAY-41-2272 converts the CO adduct of soluble guanylyl cyclase (CO-sGC) enzyme from a low- to high-output form, with respect to production of cGMP. Resonance Raman (RR) and Fourier Transform IR (FTIR) spectroscopic techniques are used to show that the CO-sGC exists as major and minor conformers, both having ν(Fe-CO) and ν(C-O) modes characteristic of 6-coordinate species. It is further shown that addition of BAY-41-2272 to the CO adduct induces the transition of some fraction of the initial CO-heme adducts into two new CO-heme complexes, the fractional conversion being dependent on the temperature One new complex displays vibrational modes characteristic of pentacoordinated CO-adduct, and its formation is not affected by temperature The second complex, although slightly different from the original CO-adducts, is hexacoordinated, and its formation is facilitated by temperature The production of substantial amts. of the 5-coordinate CO adduct upon addition of BAY-41-2272, reveals the fact that several out-of-plane heme deformation modes are simultaneously activated, an observation similar to that realized upon NO activation. While the precise nature of these modes will require elucidation by isotopic labeling expts., by analogy with earlier studies of other heme proteins, several bands associated with modes attributable to peripheral substituent deformations and methine carbon movements are implicated. The documented formation of two new forms upon addition of Bay-41-2272 (a 5-coordinate and a new 6-coordinate form) is discussed with respect to the implications for enzyme activation.
IT **256376-24-6**, BAY-41-2272
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(resonance Raman and FTIR studies of high-output forms of human soluble guanylyl cyclase reveal 5-coordinate form and new 6-coordinate form of Co adduct upon addition of Bay-41-2272 with soluble guanylyl cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



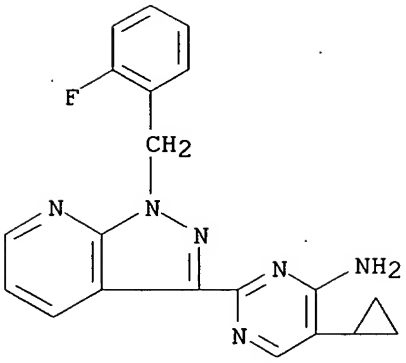
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:184188 CAPLUS
DN 142:329797
TI Inhibitory effects on human eosinophil chemotaxis in vitro by BAY 41-2272, an activator of nitric oxide-independent site of soluble guanylate cyclase
AU Thomazzi, Sara M.; Moreira, Juliana; De Nucci, Gilberto; Antunes, Edson
CS Faculty of Medical Sciences, Department of Pharmacology, UNICAMP, Campinas (SP), 13084-971, Brazil
SO Biochemical Pharmacology (2005), 69(6), 875-882
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier B.V.
DT Journal
LA English
AB This study was designed to investigate the effects of the 5-cyclopropyl-2-[1-(2-fluoro-benzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-pyrimidin-4-ylamine (BAY 41-2272) on formyl-methionyl-leucyl-phenylalanine (fMLP; 10-7 M)-induced human eosinophil chemotaxis, cyclic guanosine-3',5'-monophosphate (cGMP) and cyclic adenosine-3',5'-monophosphate (cAMP) levels. Human eosinophils were pretreated or not with 3-isobutyl-1-methyl-xanthine (IBMX; 500 μM), and then exposed to BAY 41-2272 (0.1-10.0 μM) for either short (10 min) or prolonged (90 min) time periods. Exposition of eosinophils with BAY 41-2272 for either 10 min or 90 min markedly inhibited the eosinophil chemotaxis, independently of IBMX pretreatment. Inhibition of fMLP-induced eosinophil chemotaxis by BAY 41-2272 (in absence of prior treatment with IBMX) was about of the same irresp. if cells were exposed for 10 min or 90 min with this compound In IBMX-pretreated eosinophils, the inhibition of fMLP-induced chemotaxis by BAY 41-2272 in the 10-min exposure protocols was even higher in comparison with the 90-min protocols. Incubation of IBMX-treated eosinophils for 90 min with BAY 41-2272 resulted in 2.0-2.5 times higher levels of cGMP and cAMP compared with the 10-min protocols. The BAY 41-2272-induced cGMP increases were abolished by pre-incubation of eosinophils with the soluble guanylate cyclase inhibitor 1H-[1,2,4]-oxidiazolo[4,3-a] quinoxalin-1-one (ODQ). No eosinophil toxicity was observed in any exptl. condition, according to 3-(4,5-dimethylthiazol-2-yl)-2,5 di-Ph tetrazolium bromide (MTT) assay. Our findings show that inhibitory effects of fMLP-induced human eosinophil chemotaxis by BAY 41-2272 at short-term or prolonged exposition time are accompanied by significant elevations of cGMP and cAMP, but we could not detect a clear correlation between chemotaxis inhibition and elevation of cyclic nucleotide levels.
IT **256376-24-6**, BAY 41-2272
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(inhibitory effects on human eosinophil chemotaxis in vitro by BAY 41-2272, an activator of nitric oxide-independent site of soluble guanylate cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:171754 CAPLUS
DN 142:274428
TI Localization and characterization of cGMP-immunoreactive structures in rat brain slices after NO-dependent and NO-independent stimulation of soluble guanylyl cyclase
AU Van Staveren, Wilma C. G.; Markerink-Van Ittersum, Marjanne; Steinbusch, Harry W. M.; Behrends, Soenke; De Vente, Jan
CS European Graduate School of Neuroscience (EURON), Department of Psychiatry and Neuropsychology, Division Cellular Neuroscience, UNS50, Maastricht University, Maastricht, 6200 MD, Neth.
SO Brain Research (2005), 1036(1-2), 77-89
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier B.V.
DT Journal
LA English
AB Possible differences in the localization of the cGMP response were investigated in rat brain coronal slices after in vitro incubation and NO-dependent or NO-independent stimulation of soluble guanylyl cyclase (sGC). Dose-dependent stimulation of cGMP synthesis by the NO donors, sodium nitroprusside, S-nitrosoglutathione, 3-morpholinosydnonimine and diethylamino-NONOate was studied in the somatoparietal cortex, the hippocampus and the thalamus. The cGMP accumulation was evaluated using a RIA and by measuring cGMP-immunofluorescence using image anal. All four NO donors induced similar cGMP staining patterns in the somatoparietal cortex, the hippocampus and the thalamus. NO-mediated cGMP synthesis in the cortical areas colocalized predominantly with the acetylcholine transporter and occasionally with parvalbumin (GABAergic cells) or the neuronal glutamate transporter. Incubation of the slices in the combined presence of a NO donor and the NO-independent activators YC-1 or BAY 41-2272 strongly potentiated cGMP synthesis and induced abundant cGMP-immunoreactivity in cortical GABAergic and glutamatergic cells. These findings indicate that the mechanism of NO release from the NO donors used does not determine the location of the cGMP response. The results suggest that YC-1 and BAY 41-2272 trigger a NO-sensing mechanism in cells in which the sGC is otherwise not sensitive to NO.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); BIOL (Biological study)
(cGMP-immunoreactive structures localization and characterization in rat brain slices after nitric oxide-dependent and -independent stimulation of soluble guanylyl cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

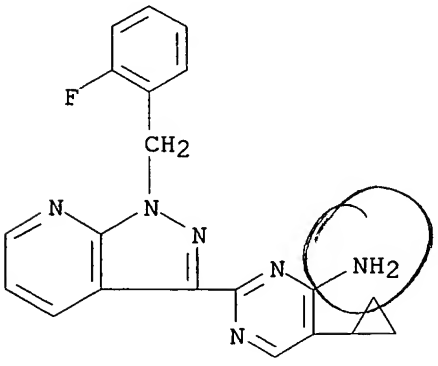
L4 ANSWER 13 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:120761 CAPLUS
DN 142:191266
TI soluble guanylate cyclase activator and ACE-inhibitor for the treatment of cardiovascular or metabolic disorders
IN Fox, David Nathan Abraham; Karran, Eric Howard
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005011727	A1	20050210	WO 2004-IB2469	20040726
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005059660	A1	20050317	US 2004-902316	20040729
PRAI	GB 2003-18094	A	20030801		
	US 2003-500748P	P	20030904		

AB The invention discloses combinations comprising (a) an activator of soluble guanylate cyclase and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating a cardiovascular or metabolic disorder, in particular hypertension or diabetes.

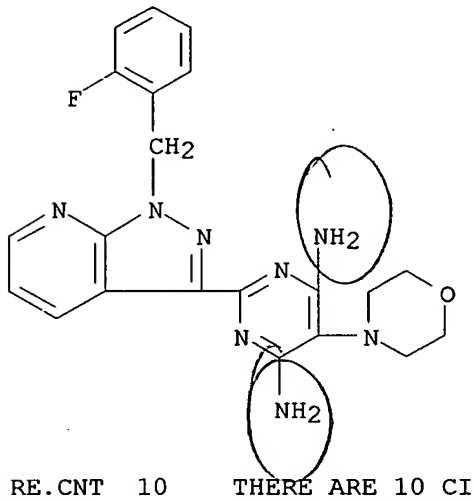
IT **256376-24-6**, BAY41-2272 **256498-66-5**, Bay41-8543
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soluble guanylate cyclase activator and ACE-inhibitor for treatment of cardiovascular or metabolic disorders)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS

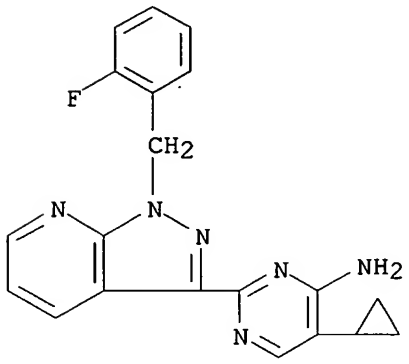
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

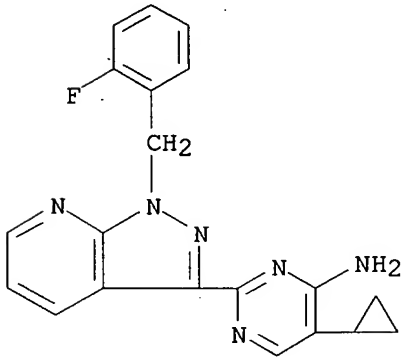
L4 ANSWER 14 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:24778 CAPLUS
DN 142:296013
TI Expression and activity of soluble guanylate cyclase in injury and repair of anti-thy1 glomerulonephritis
AU Peters, Harm; Wang, Yingrui; Loof, Tanja; Martini, Sebastian; Kron, Susanne; Kraemer, Stephanie; Neumayer, Hans-H.
CS Department of Nephrology and Center of Cardiovascular Research, Charite Medicine Berlin, Humboldt University, Berlin, Germany
SO Kidney International (2004), 66(6), 2224-2236
CODEN: KDYIA5; ISSN: 0085-2538
PB Blackwell Publishing, Inc.
DT Journal
LA English
AB Background. Activation of soluble guanylate cyclase and generation of cyclic 3',5'-guanosine monophosphate (cGMP) is the main signal transducing event of the L-arginine-nitric oxide pathway. The present study analyzes the expression and activity of the nitric oxide-cGMP signaling cascade in and the effect of the specific soluble guanylate cyclase stimulator Bay 41-2272 on the early injury and subsequent repair phase of acute anti-thy1 glomerulonephritis. Methods. Anti-thy1 glomerulonephritis was induced by OX-7 antibody injection in rats. In protocol 1 (injury), Bay 41-2272 was given starting 6 days before antibody injection. One day after disease induction, parameters of mesangial cell injury (glomerular cell number and inducible nitric oxide synthesis) were analyzed. In protocol 2 (repair), Bay 41-2272 treatment was started one day after antibody injection. On day 7, parameters of glomerular repair [glomerular matrix score, expression of transforming growth factor (TGF)-β1, fibronectin, and plasminogen-activator-inhibitor (PAI)-1, infiltration with macrophages and fibrinogen deposition (indicating platelet localization)] were determined In both protocols, tail bleeding time, systolic blood pressure, plasma cGMP levels, glomerular mRNA expression of endothelial nitric oxide synthase (eNOS), α1. and β1 soluble guanylate cyclase, and basal and nitric oxide-stimulated glomerular cGMP production were analyzed. Results. Bay 41-2272 prolonged bleeding time, reduced blood pressure, and increased plasma cGMP levels in both protocols. In the injury experiment, disease induction increased inducible nitric oxide synthesis and reduced glomerular cell number, while expression and activity of soluble guanylate cyclase was almost completely diminished. Bay 41-2272 did not affect parameters of mesangial cell injury and glomerular soluble guanylate cyclase expression and activity. In the repair protocol, expression and activity of soluble guanylate cyclase was markedly increased by disease. Bay 41-2272 further enhanced soluble guanylate cyclase expression and activity. This went along with significant redns. in proteinuria, glomerular matrix accumulation, expression of TGF-β1, fibronectin, and PAI-1, macrophage infiltration and fibrinogen deposition as compared to the untreated anti-thy1 animals. Conclusion. Glomerular nitric oxide signaling via cGMP is markedly impaired during injury of anti-thy1 glomerulonephritis, while it is highly up-regulated during subsequent repair. Further pharmacol. soluble guanylate cyclase stimulation limits glomerular TGF-β overexpression and matrix expansion, suggesting that the soluble guanylate cyclase enzyme represents an important antifibrotic pathway in glomerular disease.
IT **256376-24-6**, Bay 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression and activity of soluble guanylate cyclase in injury and repair of anti-thy1 glomerulonephritis)
RN 256376-24-6 CAPLUS

CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

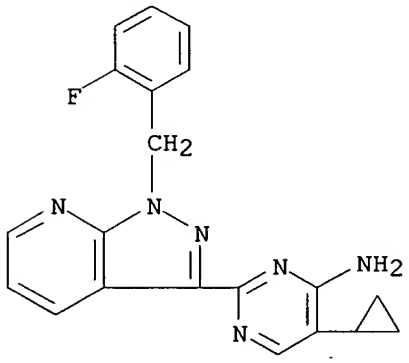


RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1009105 CAPLUS
DN 142:233190
TI A comparative study of sildenafil, NCX-911 and BAY41-2272 on the anococcygeus muscle of diabetic rats
AU Kalsi, Jasjit S.; Ralph, David J.; Madge, David J.; Kell, Phil D.; Cellek, Selim
CS Wolfson Institute for Biomedical Research, University College London, London, WC2E 6BT, UK
SO International Journal of Impotence Research (2004), 16(6), 479-485
CODEN: IJIRFB; ISSN: 0955-9930
PB Nature Publishing Group
DT Journal
LA English
AB We compared the effects of a nitric oxide (NO)-releasing sildenafil (NCX-911), NO-independent soluble guanylate cyclase activator (BAY41-2272) and sildenafil on the anococcygeus muscle from streptozotocin-induced 16-wk diabetic rats. NCX-911, BAY41-2272 and sildenafil reduced the phenylephrine-induced tone in the control group (EC50=1088.8±165.0, 151.6±9.3 and 827.1±167.3 nM, resp.). The potencies of NCX-911 and BAY41-2272 were not altered, but that of sildenafil was significantly reduced in the diabetic group. EC50 values for NCX-911, BAY41-2272 and sildenafil in the diabetic group were 1765.9±303.5, 209.7±27.3 and 2842.2±640.3 nM, resp. ($P<0.05$ for sildenafil). Nitrergic relaxation responses were significantly decreased in the diabetic group. The remaining nitrergic relaxation responses were potentiated by BAY41-2272 but not by sildenafil or NCX-911. These results confirm that endogenous NO derived from nitrergic nerves is significantly decreased in diabetes, and suggest that NO-releasing PDE5 inhibitors and NO-independent soluble guanylate cyclase activators could be more useful than PDE5 inhibitors in the treatment of ED in long-term diabetes.
IT **256376-24-6**, BAY41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY41-2272 had significant potency to reduce phenylephrine-induced tone, to reverse reduction in nitrergic response in anococcygeus muscle of diabetic rat with severe nitric oxide deficiency suggesting use in erectile dysfunction)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

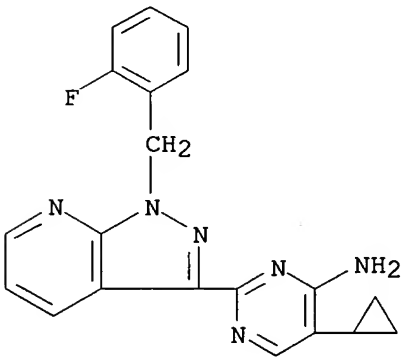


L4 ANSWER 16 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:922044 CAPLUS
DN 142:348546
TI Effects of the sGC stimulator BAY 41-2272 are not mediated by phosphodiesterase 5 inhibition. Reply to comments
AU Mullershausen, Florian; Russwurm, Michael; Friebe, Andreas; Koesling, Doris
CS Med. Fak., Inst. Pharmakol. Toxikol., Germany
SO Circulation (2004), 110(12), e320-e321
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB A polemic in response to Bischoff and Stasch (Circulation 2004, 110, e320) is given. The effects of BAY 41-2272 on platelet cGMP cannot be solely explained by activation of guanylyl cyclase (GC) but by the combined action on GC and phosphodiesterase type 5.
IT **256376-24-6**, BAY 41-2272
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(guanylyl cyclase and phosphodiesterase 5 in mechanism of BAY 41-2272)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



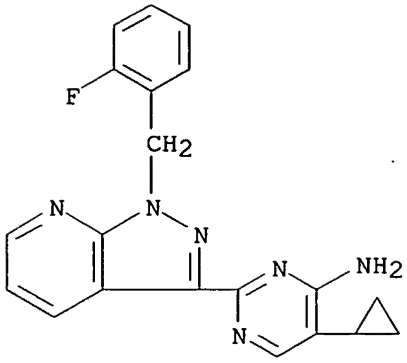
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:922042 CAPLUS
DN 142:348545
TI Effects of the sGC stimulator BAY 41-2272 are not mediated by phosphodiesterase 5 inhibition. Comments
AU Bischoff, Erwin; Stasch, Johannes-Peter
CS Cardiovascular Research, Bayer HealthCare, Wuppertal, Germany
SO Circulation (2004), 110(12), e320
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB A polemic in response to Mullershausen et al. (Circulation 2004, 109, 1711-1713) is given. Bischoff and Stasch claim that Mullershausen et al. overestimated the potency of BAY 41-2272 on phosphodiesterase type 5 and underestimated its potency on guanylyl cyclase.
IT **256376-24-6**, BAY 41-2272
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(BAY 41-2272 effect on phosphodiesterase 5 and guanylyl cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:815724 CAPLUS
DN 142:169648
TI Soluble Guanylate Cyclase Activator Reverses Acute Pulmonary Hypertension and Augments the Pulmonary Vasodilator Response to Inhaled Nitric Oxide in Awake Lambs
AU Evgenov, Oleg V.; Ichinose, Fumito; Evgenov, Natalia V.; Gnoth, Mark J.; Falkowski, George E.; Chang, Yuchiao; Bloch, Kenneth D.; Zapol, Warren M.
CS Department of Anesthesia and Critical Care, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
SO Circulation (2004), 110(15), 2253-2259
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Background: Inhaled nitric oxide (NO) is a potent and selective pulmonary vasodilator, which induces cGMP synthesis by activating soluble guanylate cyclase (sGC) in ventilated lung regions. Carbon monoxide (CO) has also been proposed to influence smooth muscle tone via activation of sGC. We examined whether direct stimulation of sGC by BAY 41-2272 would produce pulmonary vasodilation and augment the pulmonary responses to inhaled NO or CO. Methods and Results: In awake, instrumented lambs, the thromboxane analog U-46619 was i.v. administered to increase mean pulmonary arterial pressure to 35 mm Hg. I.v. infusion of BAY 41-2272 (0.03, 0.1, and 0.3 mg · kg-1 · h-1) reduced mean pulmonary arterial pressure and pulmonary vascular resistance and increased transpulmonary cGMP release in a dose-dependent manner. Larger doses of BAY 41-2272 also produced systemic vasodilation and elevated the cardiac index. Nω-nitro-L-arginine Me ester abolished the systemic but not the pulmonary vasodilator effects of BAY 41-2272. Furthermore, infusing BAY 41-2272 at 0.1 mg · kg-1 · h-1 potentiated and prolonged the pulmonary vasodilation induced by inhaled NO (2, 10, and 20 ppm). In contrast, inhaled CO (50, 250, and 500 ppm) had no effect on U-46619-induced pulmonary vasoconstriction before or during administration of BAY 41-2272. Conclusions: In lambs with acute pulmonary hypertension, BAY 41-2272 is a potent pulmonary vasodilator that augments and prolongs the pulmonary vasodilator response to inhaled NO. Direct pharmacol. stimulation of sGC, either alone or in combination with inhaled NO, may provide a novel approach for the treatment of pulmonary hypertension.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sGC activator BAY 41-2272 counteracted U-46619-induced acute PH, increased transpulmonary cGMP release, enhanced and prolonged pulmonary vasodilator response to inhaled NO but not to CO in lambs)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

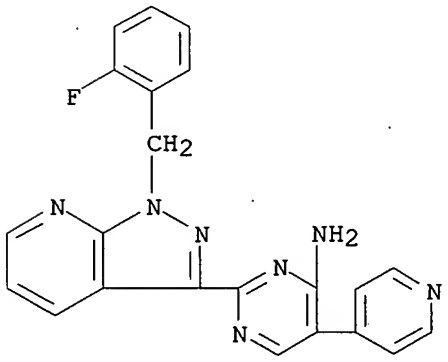


RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

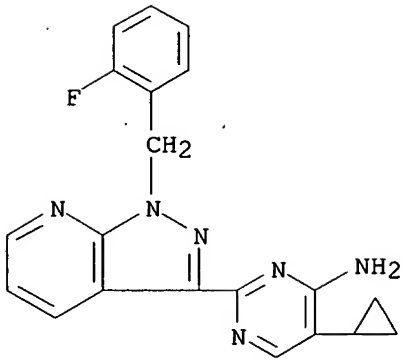
L4 ANSWER 19 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:778543 CAPLUS
DN 141:271569
TI Use of stimulators of soluble guanylate cyclase for the treatment of pulmonary hypertension
IN Weigand, Stefan; Frey, Reiner; Stasch, Johannes-Peter
PA Bayer Healthcare A.-G., Germany
SO Ger. Offen., 5 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10310908	A1	20040923	DE 2003-10310908	20030313
PRAI DE 2003-10310908		20030313		

OS MARPAT 141:271569
AB The invention discloses the use of stimulators of soluble guanylate cyclase for the production of a medicament for treatment of pulmonary hypertension. Compds. of the invention include I (R1 = 4-pyridinyl, 3-pyridinyl; R2 = H, NH2, Cl).
IT **402595-29-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soluble guanylate cyclase stimulators for treatment of pulmonary hypertension)
RN 402595-29-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:288993 CAPLUS
DN 141:360387
TI Inhibition of Phosphodiesterase Type 5 by the Activator of Nitric Oxide-Sensitive Guanylyl Cyclase BAY 41-2272
AU Mullershausen, Florian; Russwurm, Michael; Friebe, Andreas; Koesling, Doris
CS Medizinische Fakultaet, Institut fuer Pharmakologie und Toxikologie, Ruhr-Universitaet Bochum, Bochum, 44780, Germany
SO Circulation (2004), 109(14), 1711-1713
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Background- By the formation of cGMP, nitric oxide (NO)-sensitive guanylyl cyclase (GC) acts as the effector for the signaling mol. NO and mediates the relaxation of vascular smooth muscle and the inhibition of platelet aggregation. The compds. YC-1 and BAY 41-2272 are regarded as NO-independent activators and sensitizers of NO-sensitive GC. In vivo effects, for example, lowering blood pressure and prolonging tail-bleeding times, turn the compds. into promising candidates for the therapy of cardiovascular diseases. However, YC-1 has also been shown to inhibit the major cGMP-degrading enzyme phosphodiesterase type 5 (PDE5). The synergistic properties of YC-1 on cGMP formation and degradation lead to an excessive NO-induced cGMP accumulation in cells, explaining the observed physiol. effects. We assessed a potential inhibition of PDE5 by the new GC activator BAY 41-2272. Methods and Results- The effects of BAY 41-2272 on NO-sensitive GC and PDE5 activities were tested in vitro. BAY 41-2272 not only sensitized NO-sensitive GC toward activation by NO but also, with comparable potency, inhibited cGMP degradation by PDE5. In intact platelets, BAY 41-2272 greatly potentiated the NO-induced cGMP response that was caused by a synergistic effect of BAY 41-2272 on cGMP formation and degradation Conclusions- The physiol. effects of BAY 41-2272, which are commonly ascribed to the NO-independent activation of NO-sensitive GC, are rather due to the synergism of sensitization of NO-sensitive GC and inhibition of PDE5.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 41-2272 not only sensitized NO-sensitive GC toward activation by NO but also inhibited cGMP degradation by PDE5 thereby elevating cGMP levels by synergistic effect in human platelets)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:218477 CAPLUS
DN 140:253560
TI Preparation of pyrazoles as inhibitors of cGMP degradation for the treatment of treatment of cardiovascular diseases
IN Feurer, Achim; Stasch, Johannes-Peter; Weigand, Stefan; Kern, Armin
PA Bayer A.-G., Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10242941	A1	20040318	DE 2002-10242941	20020916
WO 2004031187	A1	20040415	WO 2003-EP9759	20030903

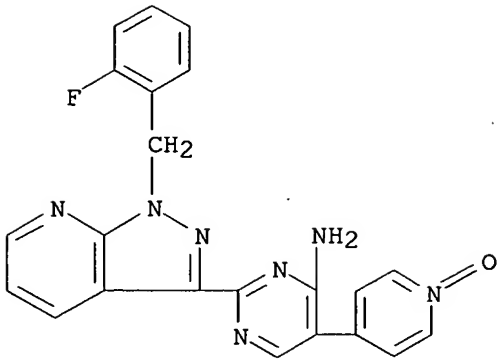
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2002-10242941 A 20020916

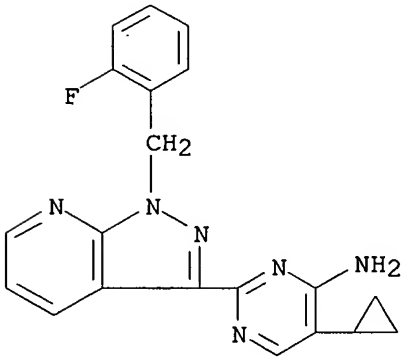
AB Title compound I was prepared from 2-fluorophenylhydrazine and 4-pyridylacetonitrile. For example, condensation of carboximidamide II hydrochloride, e.g., prepared from 2-fluorophenylhydrazine in 6-steps, and propenenitrile III, e.g., prepared from 4-pyridylacetonitrile in 2-steps, afforded compound I in 31%. In aorta vessel relaxation studies, pyrazole I exhibited an IC50 value of 286 nM. Compound I was claimed useful for the treatment of cardiovascular diseases.

IT **671241-02-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazoles as inhibitors of cGMP degradation for the treatment of
central nervous system diseases)

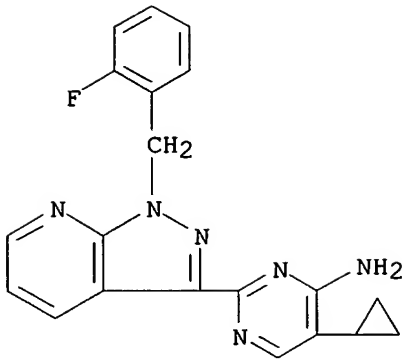
RN 671241-02-4 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(1-oxido-4-pyridinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:146763 CAPLUS
DN 140:299396
TI Functional Characterization of Nitric Oxide and YC-1 Activation of Soluble Guanylyl Cyclase: Structural Implication for the YC-1 Binding Site?
AU Lamothe, Maria; Chang, Fu-Jung; Balashova, Nataliya; Shirokov, Roman; Beuve, Annie
CS Department of Pharmacology and Physiology New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, NJ, 07103, USA
SO Biochemistry (2004), 43(11), 3039-3048
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Soluble guanylyl cyclase (sGC) is a heterodimeric enzyme formed by an α subunit and a β subunit, the latter containing the heme where nitric oxide (NO) binds. When NO binds, the basal activity of sGC is increased several hundred fold. SGC activity is also increased by YC-1, a benzylindazole allosteric activator. In the presence of NO, YC-1 synergistically increases the catalytic activity of sGC by enhancing the affinity of NO for the heme. The site of interaction of YC-1 with sGC is unknown. The authors conducted a mutational anal. to identify the binding site and to determine what residues were involved in the propagation of NO and/or YC-1 activation. Because guanylyl cyclases (GCs) and adenylyl cyclases (ACs) are homologous, the authors used the three-dimensional structure of AC to guide the mutagenesis. Biochem. anal. of purified mutants revealed that YC-1 increases the catalytic activity not only by increasing the NO affinity but also by increasing the efficacy of NO. Effects of YC-1 on NO affinity and efficacy were dissociated by single-point mutations implying that YC-1 has, at least, two types of interaction with sGC. A structural model predicts that YC-1 may adopt two configurations in one site that is pseudosym. with the GTP binding site and equivalent to the forskolin site in AC.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand; functional characterization of nitric oxide and YC-1 activation of soluble guanylyl cyclase in relation to YC-1 allosteric sitesq)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:131082 CAPLUS
DN 140:216126
TI Antiinflammatory activity of soluble guanylate cyclase: cGMP-dependent down-regulation of P-selectin expression and leukocyte recruitment
AU Ahluwalia, Amrita; Foster, Paul; Scotland, Ramona S.; McLean, Peter G.; Mathur, Anthony; Perretti, Mauro; Moncada, Salvador; Hobbs, Adrian J.
CS William Harvey Research Institute, London, EC1M 6BQ, UK
SO Proceedings of the National Academy of Sciences of the United States of America (2004), 101(5), 1386-1391
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Nitric oxide (NO) production by the vascular endothelium maintains an essential antiinflammatory, cytoprotective influence on the blood vessel wall. A key component of this activity is attributed to prevention of leukocyte-endothelial cell interactions, yet the underlying mechanisms remain unclear. The NO receptor, soluble guanylate cyclase (sGC), is expressed in endothelial cells but fulfils an unknown function. Therefore, we used intravital microscopy in mesenteric postcapillary venules from WT and endothelial nitric oxide synthase (eNOS) knockout (eNOS-/-) mice, and an sGC activator (BAY 41-2272), to investigate a potential role for sGC in the regulation of adhesion mol. expression and leukocyte recruitment. Leukocyte rolling and adhesion was 6-fold greater in eNOS-/- than WT animals. BAY 41-2272 and the NO-donor, diethylamine-NONOate, reduced leukocyte rolling and adhesion in eNOS-/- mice to levels observed in WT animals. These effects were blocked by the sGC inhibitor ODQ [1H-(1,2,4)oxadiazolo(4,3-a)quinoxalin-1-one], which itself caused a 6-fold increase in leukocyte rolling and adhesion in WT mice. Increased leukocyte rolling and adhesion in IL-1β-treated mice was also inhibited by BAY 41-2272. Fluorescence-activated cell sorting anal. in vitro and a specific P-selectin neutralizing antibody in vivo revealed that selective down-regulation of P-selectin expression accounted for the antiadhesive effects of sGC activation. These data demonstrate that sGC plays a key antiinflammatory role by inhibiting P-selectin expression and leukocyte recruitment.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-nitric oxide-based soluble guanylate cyclase activator)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

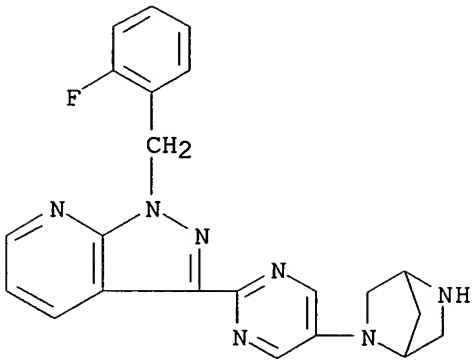


RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

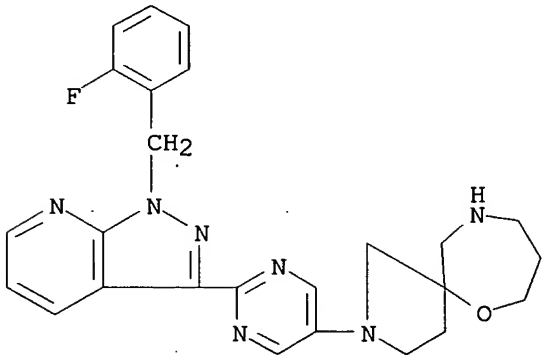
L4 ANSWER 24 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:80686 CAPLUS
DN 140:146157
TI Preparation of pyrazolopyridinylpyrimidines as inhibitors of cGMP degradation for the treatment of central nervous system diseases
IN Feurer, Achim; Luithle, Joachim; Wirtz, Stephan-nicholas; Koenig, Gerhard; Stasch, Johannes-peter; Stahl, Elke; Schreiber, Rudy; Wunder, Frank; Lang, Dieter
PA Bayer Healthcare Ag, Germany
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009589	A1	20040129	WO 2003-EP7238	20030707
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10232572	A1	20040205	DE 2002-10232572	20020718
	CA 2492723	AA	20040129	CA 2003-2492723	20030707
	EP 1525202	A1	20050427	EP 2003-764943	20030707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	DE 2002-10232572	A	20020718		
	WO 2003-EP7238	W	20030707		

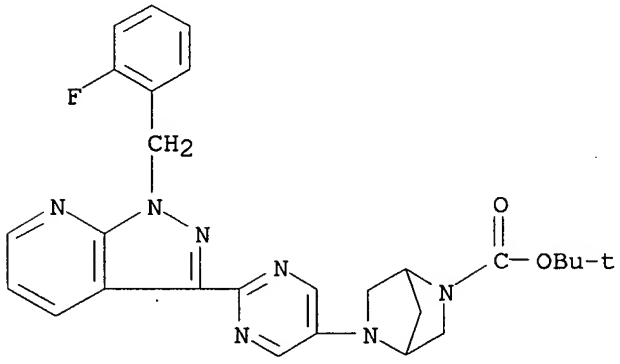
OS MARPAT 140:146157
AB Title compds. I [R1 = (un)substituted aryl, heteroaryl, benzodioxole, etc.] and their pharmaceutically acceptable salts were prepared For example, palladium mediated coupling of bromide I [R1 = Br], e.g., prepared from 2-fluorobenzylhydrazine in 6-steps, and cyclohexanone afforded pyrazolopyridinylpyrimidine II in 29% yield. In cGMP degradation inhibition assays, 10-examples of compds. I exhibited a significant increase (sic) in cGMP concentration at 0.27-1.2 μM inhibitor concentration Compds. I are claimed useful for the treatment of learning, concentration and perception disorders.
IT **651339-98-9P 651340-02-2P 651341-09-2P**
651341-11-6P 651341-13-8P 651341-17-2P
651341-21-8P 651341-24-1P 651341-38-7P
651341-40-1P 651341-59-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of pyrazolopyridinylpyrimidines as inhibitors of cGMP degradation for the treatment of central nervous system diseases)
RN 651339-98-9 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



RN 651340-02-2 CAPLUS
CN 6-Oxa-2,10-diazaspiro[4.6]undecane, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)

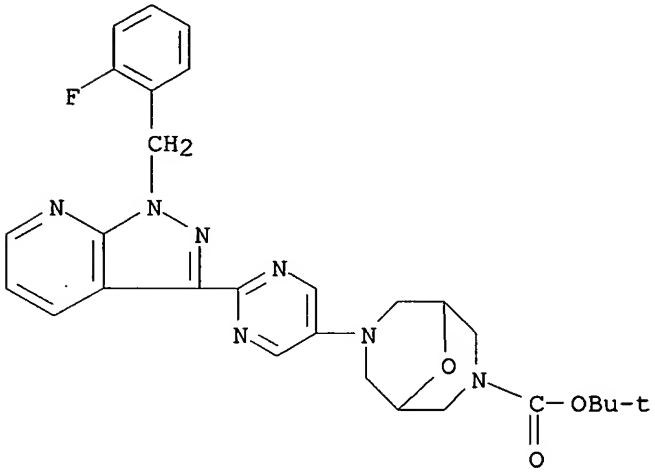


RN 651341-09-2 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane-2-carboxylic acid, 5-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

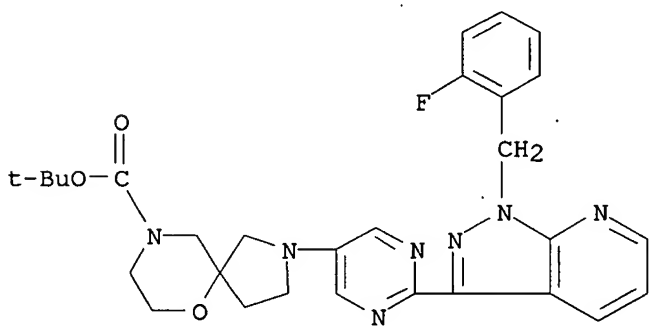


RN 651341-11-6 CAPLUS

CN 9-Oxa-3,7-diazabicyclo[3.3.1]nonane-3-carboxylic acid, 7-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

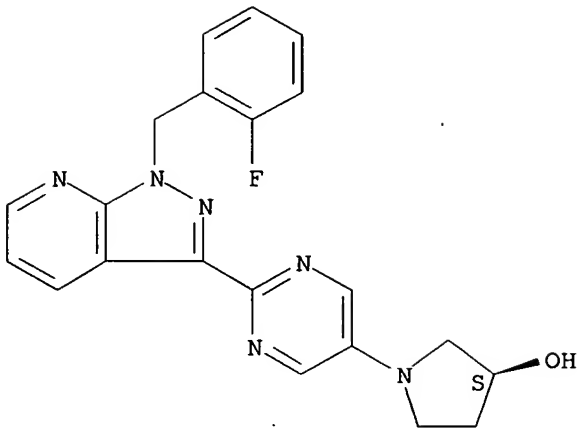


RN 651341-13-8 CAPLUS
CN 6-Oxa-2,9-diazaspiro[4.5]decane-9-carboxylic acid, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

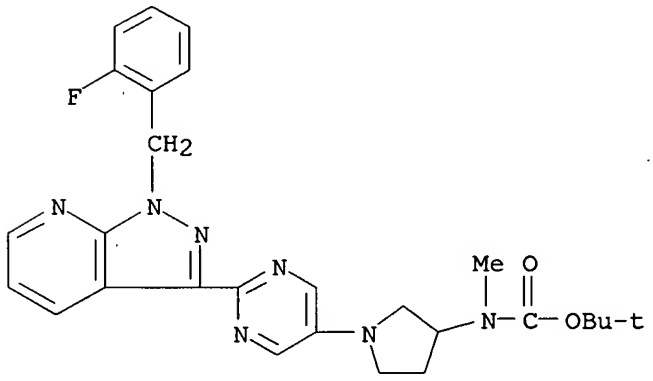


RN 651341-17-2 CAPLUS
CN 3-Pyrrolidinol, 1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

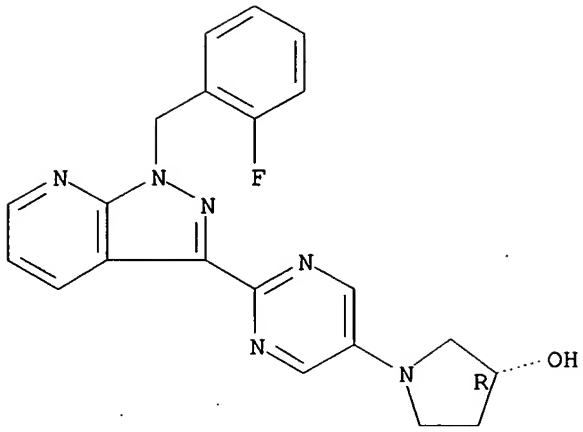


RN 651341-21-8 CAPLUS
CN Carbamic acid, [1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-3-pyrrolidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

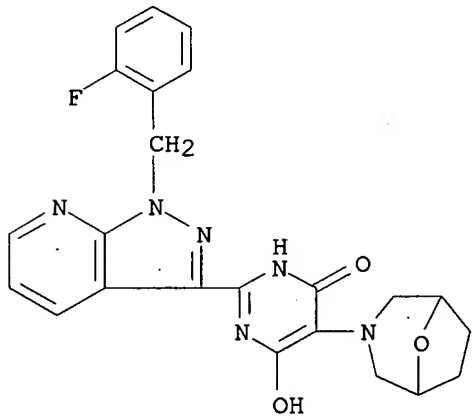


RN 651341-24-1 CAPLUS
CN 3-Pyrrolidinol, 1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, (3R)- (9CI) (CA INDEX NAME)

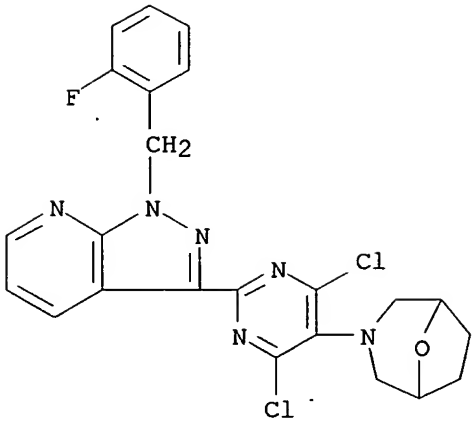
Absolute stereochemistry.



RN 651341-38-7 CAPLUS
CN 4(1H)-Pyrimidinone, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-6-hydroxy-5-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- (9CI) (CA INDEX NAME)

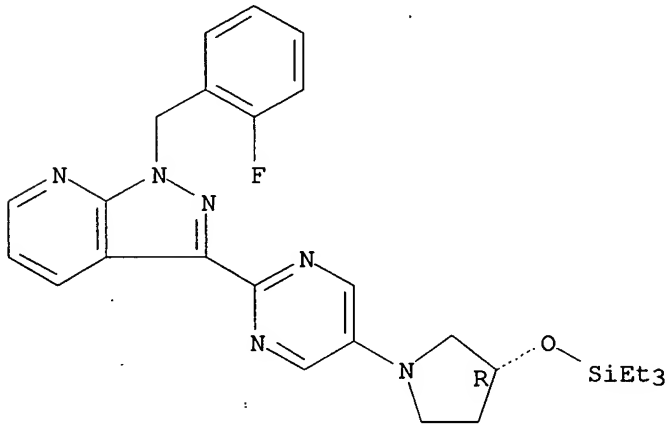


RN 651341-40-1 CAPLUS
CN 8-Oxa-3-azabicyclo[3.2.1]octane, 3-[4,6-dichloro-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



RN 651341-59-2 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-[(3R)-3-[(triethylsilyl)oxy]-1-pyrrolidinyl]-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

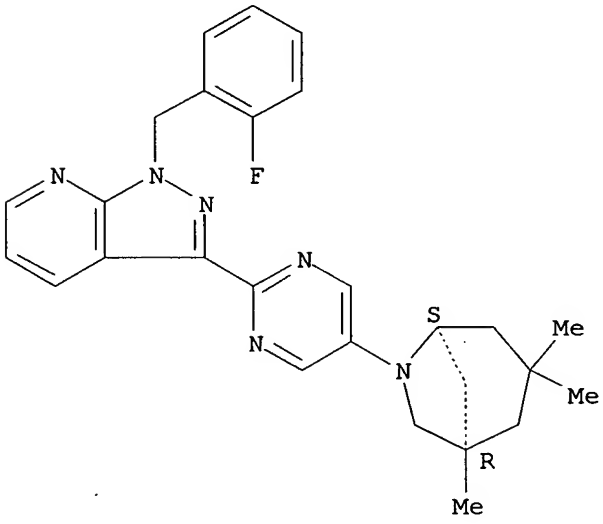
Absolute stereochemistry.



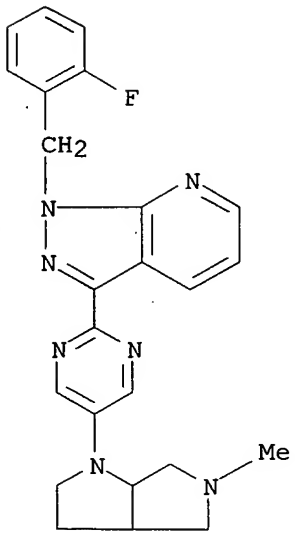
IT **651339-80-9P 651339-82-1P 651339-85-4P**
651339-87-6P 651339-89-8P 651339-91-2P
651339-93-4P 651339-96-7P 651340-00-0P
651340-05-5P 651340-07-7P 651340-10-2P
651340-13-5P 651340-16-8P 651340-19-1P
651340-22-6P 651340-25-9P 651340-28-2P
651340-31-7P 651340-34-0P 651340-37-3P
651340-39-5P 651340-42-0P 651340-45-3P
651340-47-5P 651340-49-7P 651340-52-2P
651340-55-5P 651340-58-8P 651340-61-3P
651340-65-7P 651340-68-0P 651340-71-5P
651340-74-8P 651340-78-2P 651340-81-7P
651340-84-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of pyrazolopyridinylpyrimidines as inhibitors of
cGMP degradation for the treatment of central nervous system diseases)
RN 651339-80-9 CAPLUS
CN 6-Azabicyclo[3.2.1]octane, 6-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-1,3,3-trimethyl-, (1R,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

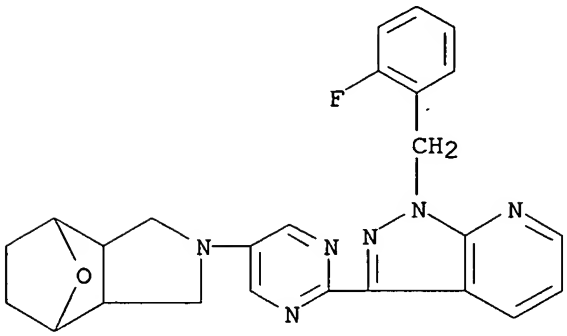


RN 651339-82-1 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(hexahydro-5-methylpyrrolo[3,4-b]pyrrol-1(2H)-yl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

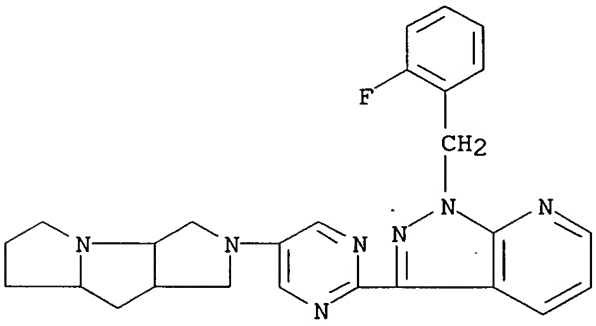


RN 651339-85-4 CAPLUS

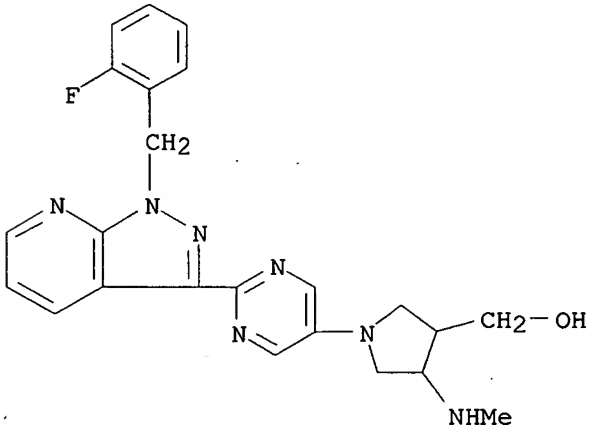
CN 4,7-Epoxy-1H-isoindole, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]octahydro- (9CI) (CA INDEX NAME)



RN 651339-87-6 CAPLUS
CN Pyrrolo[3,4-b]pyrrolizine, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]decahydro- (9CI) (CA INDEX NAME)

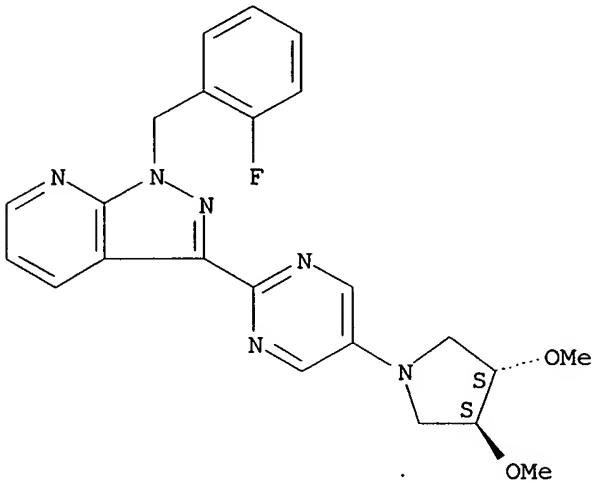


RN 651339-89-8 CAPLUS
CN 3-Pyrrolidinemethanol, 1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-4-(methylamino)- (9CI) (CA INDEX NAME)



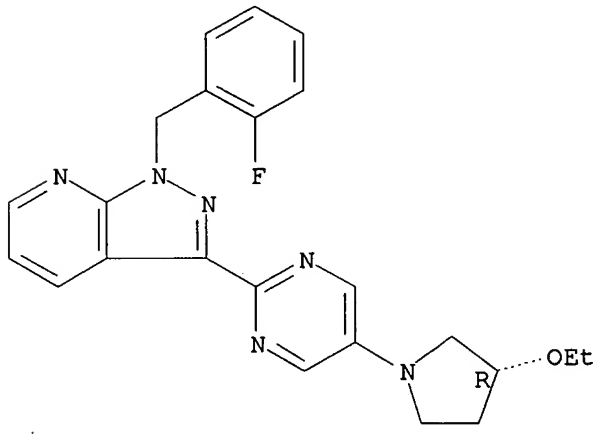
RN 651339-91-2 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-[(3R,4R)-3,4-dimethoxy-1-pyrrolidinyl]-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



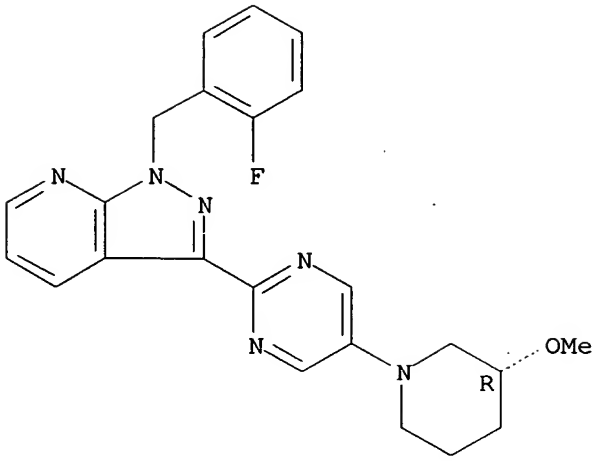
RN 651339-93-4 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-[(3R)-3-ethoxy-1-pyrrolidinyl]-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

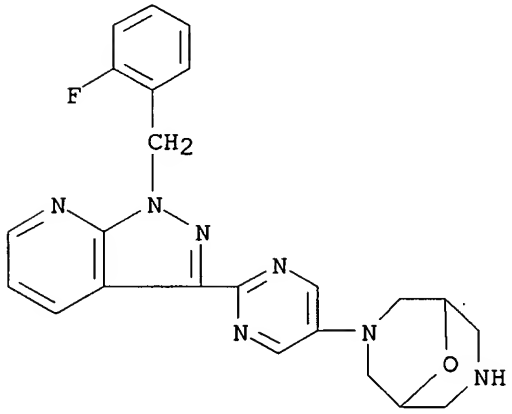


RN 651339-96-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-[(3R)-3-methoxy-1-piperidinyl]-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

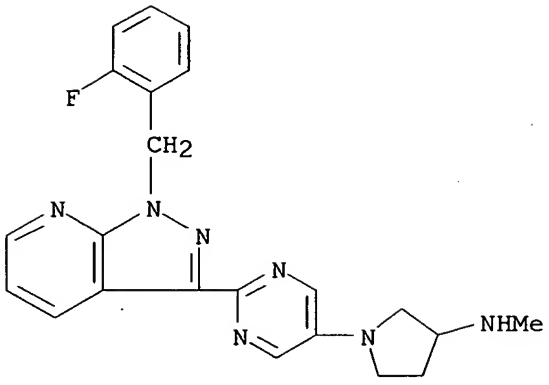
Absolute stereochemistry.



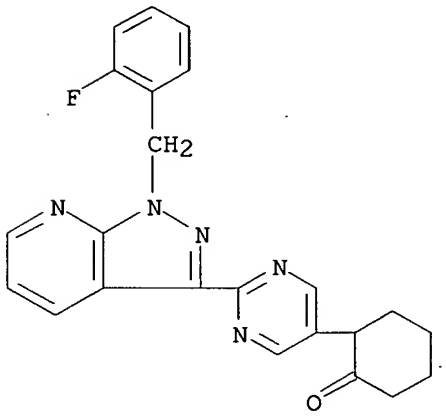
RN 651340-00-0 CAPLUS
CN 9-Oxa-3,7-diazabicyclo[3.3.1]nonane, 3-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



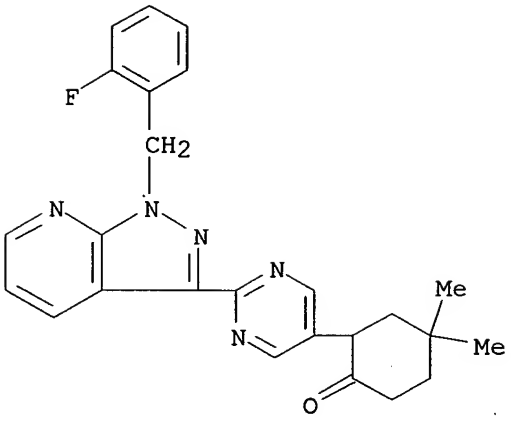
RN 651340-05-5 CAPLUS
CN 3-Pyrrolidinamine, 1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-N-methyl- (9CI) (CA INDEX NAME)



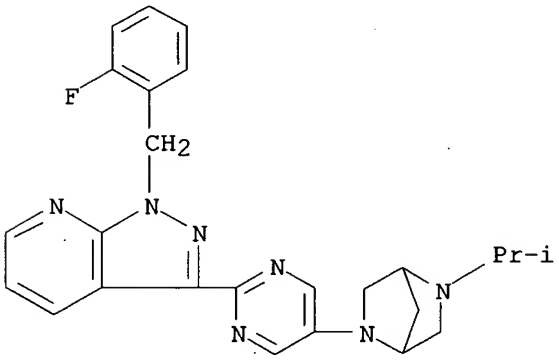
RN 651340-07-7 CAPLUS
CN Cyclohexanone, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



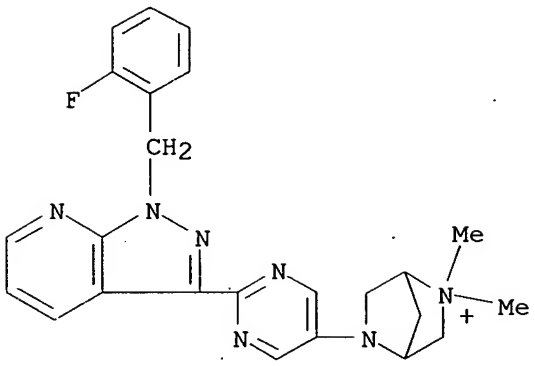
RN 651340-10-2 CAPLUS
CN Cyclohexanone, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



RN 651340-13-5 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5-(1-methylethyl)- (9CI) (CA INDEX NAME)

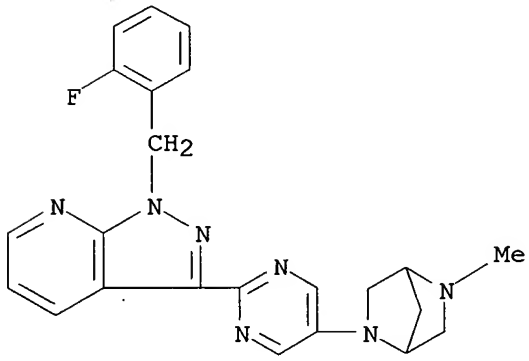


RN 651340-16-8 CAPLUS
CN 5-Aza-2-azoniabicyclo[2.2.1]heptane, 5-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-2,2-dimethyl-, chloride (9CI) (CA INDEX NAME)

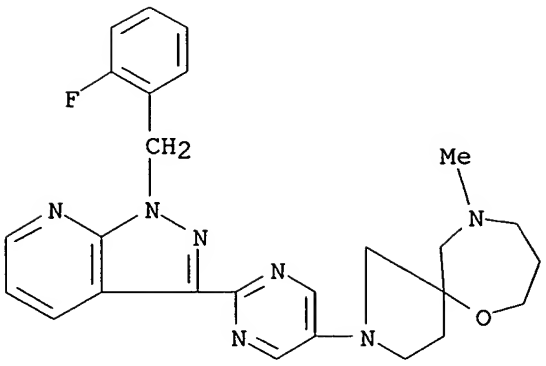


● Cl^-

RN 651340-19-1 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5-methyl- (9CI) (CA INDEX NAME)

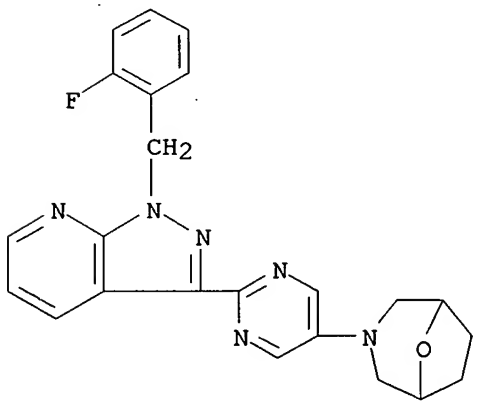


RN 651340-22-6 CAPLUS
CN 6-Oxa-2,10-diazaspiro[4.6]undecane, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-10-methyl-, hydrochloride (9CI) (CA INDEX NAME)



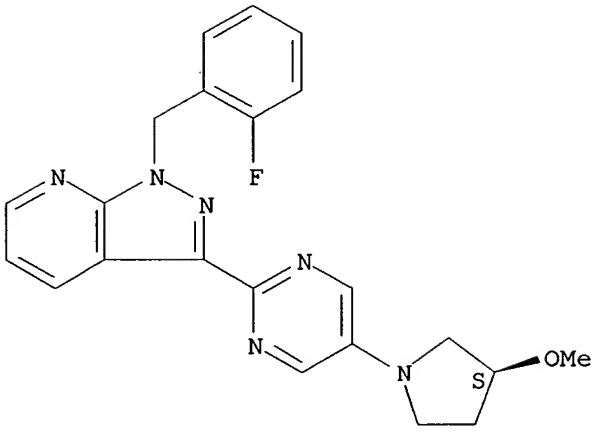
● x HCl

RN 651340-25-9 CAPLUS
CN 8-Oxa-3-azabicyclo[3.2.1]octane, 3-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



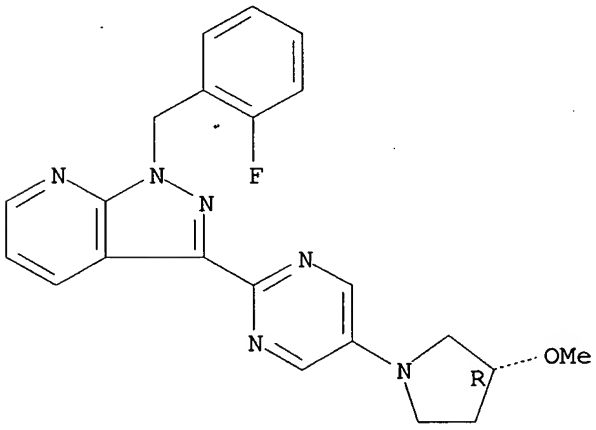
RN 651340-28-2 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-[(3S)-3-methoxy-1-pyrrolidinyl]-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

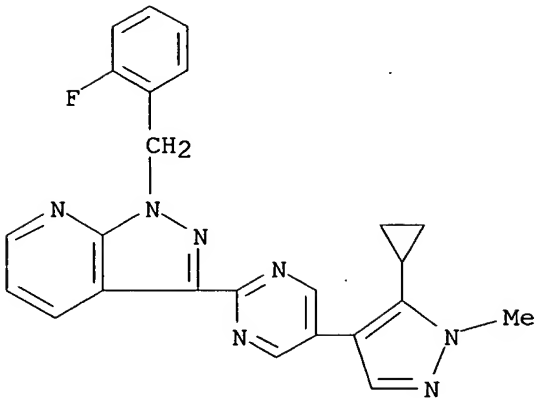


RN 651340-31-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-[(3R)-3-methoxy-1-pyrrolidinyl]-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

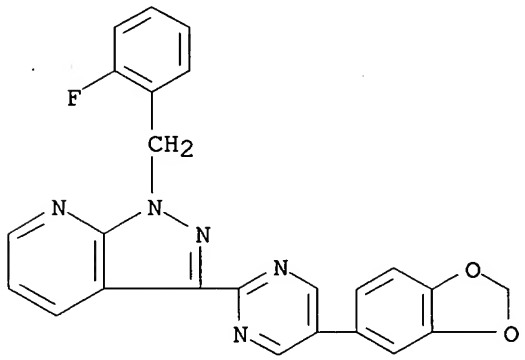
Absolute stereochemistry.



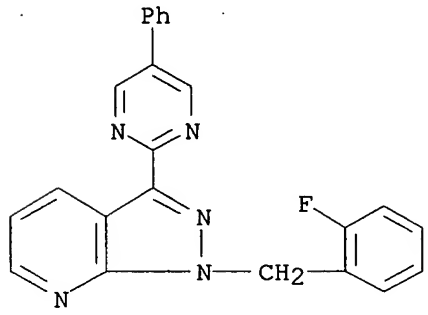
RN 651340-34-0 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-(5-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



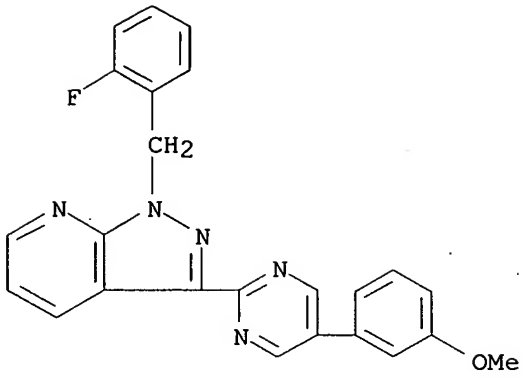
RN 651340-37-3 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-(1,3-benzodioxol-5-yl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



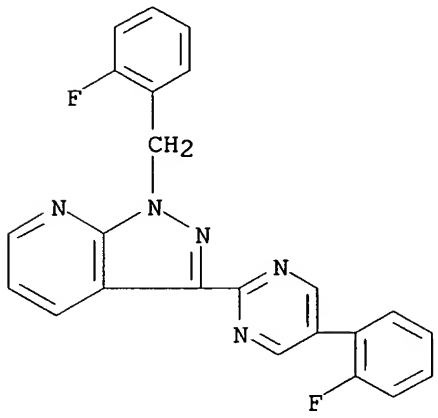
RN 651340-39-5 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-(5-phenyl-2-pyrimidinyl)- (9CI) (CA INDEX NAME)



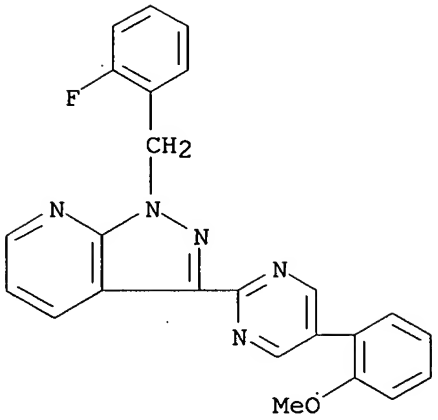
RN 651340-42-0 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(3-methoxyphenyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



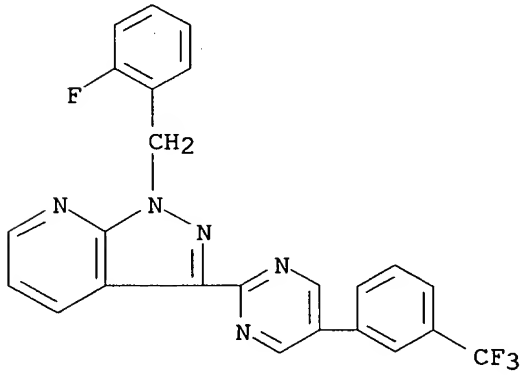
RN 651340-45-3 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(2-fluorophenyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



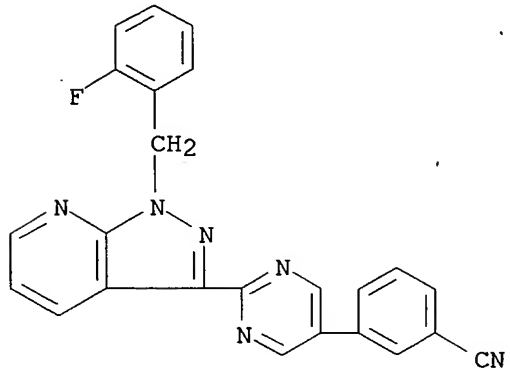
RN 651340-47-5 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(2-methoxyphenyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



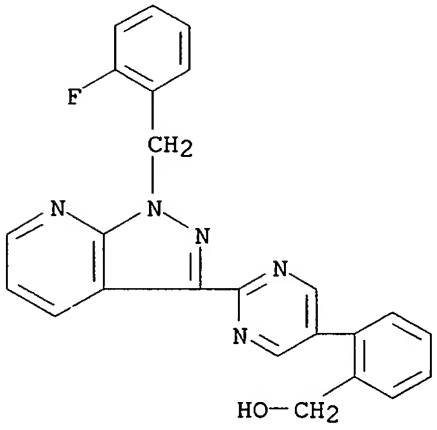
RN 651340-49-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-[3-(trifluoromethyl)phenyl]-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



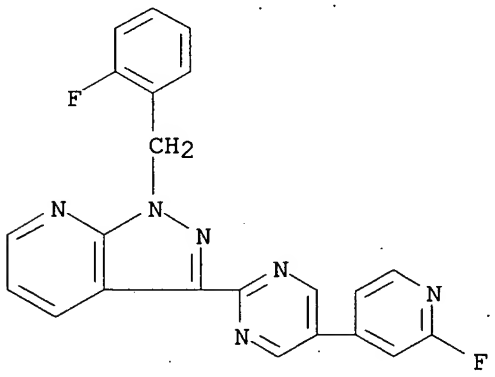
RN 651340-52-2 CAPLUS
CN Benzonitrile, 3-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



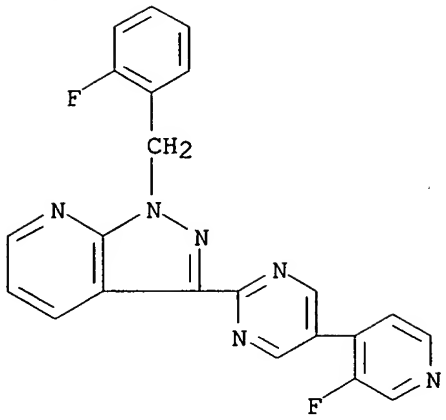
RN 651340-55-5 CAPLUS
CN Benzenemethanol, 2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



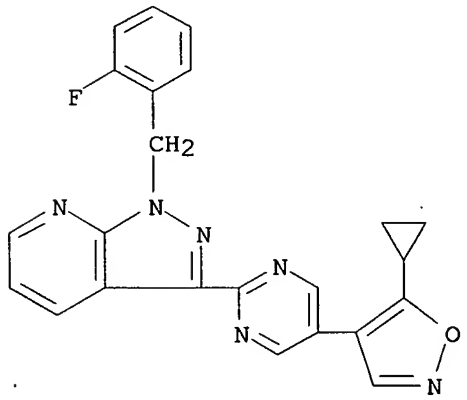
RN 651340-58-8 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(2-fluoro-4-pyridinyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



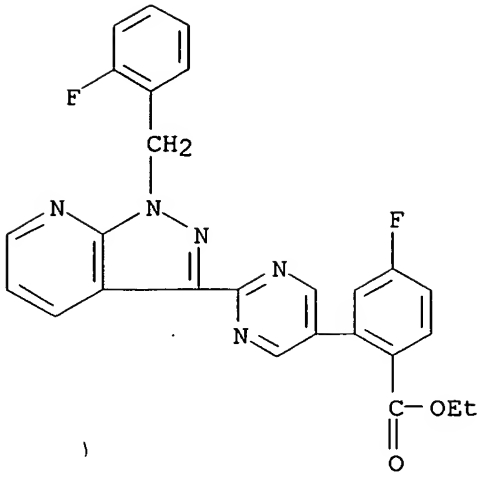
RN 651340-61-3 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(3-fluoro-4-pyridinyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



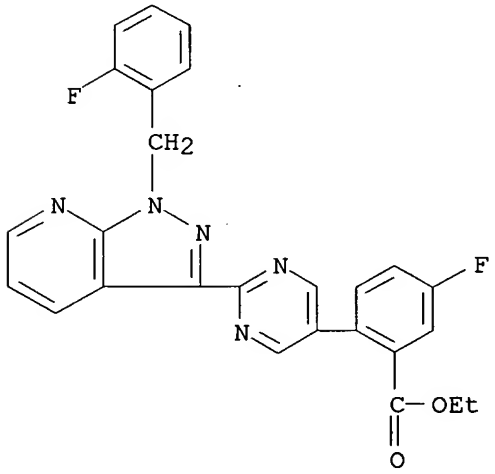
RN 651340-65-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-(5-cyclopropyl-4-isoxazolyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



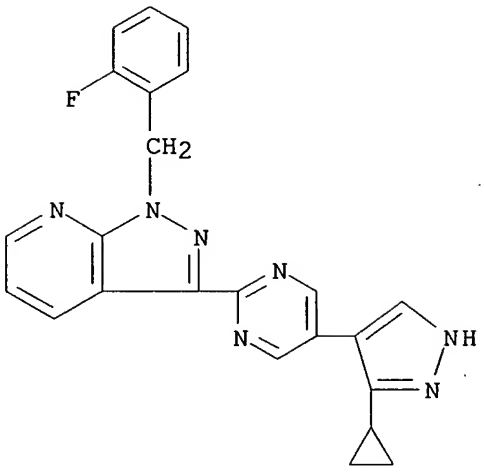
RN 651340-68-0 CAPLUS
CN Benzoic acid, 4-fluoro-2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, ethyl ester (9CI) (CA INDEX NAME)



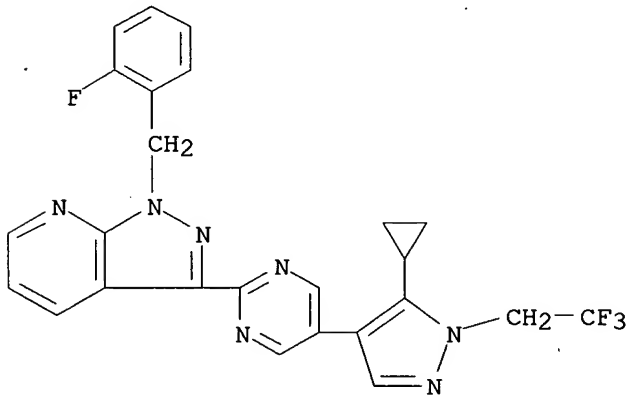
RN 651340-71-5 CAPLUS
CN Benzoic acid, 5-fluoro-2-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-, ethyl ester (9CI) (CA INDEX NAME)



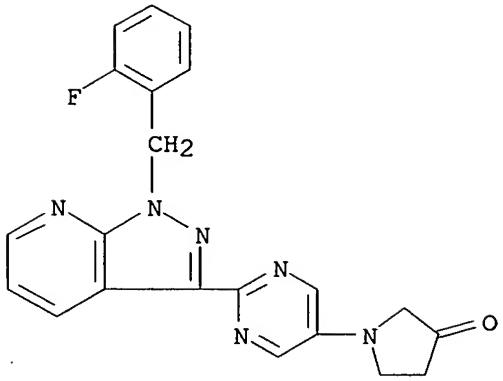
RN 651340-74-8 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-(3-cyclopropyl-1H-pyrazol-4-yl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



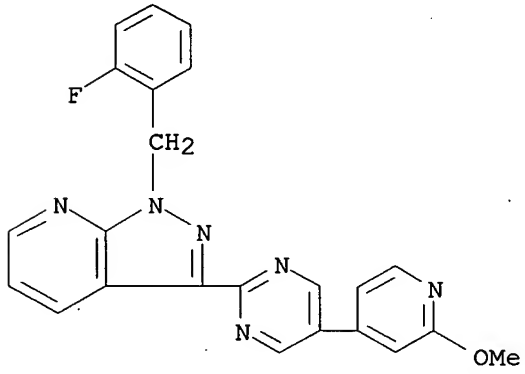
RN 651340-78-2 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-[5-cyclopropyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 651340-81-7 CAPLUS
CN 3-Pyrrolidinone, 1-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



RN 651340-84-0 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(2-methoxy-4-pyridinyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)

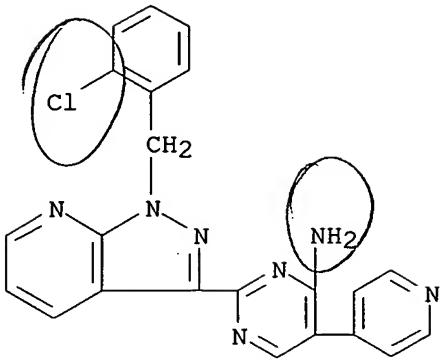


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

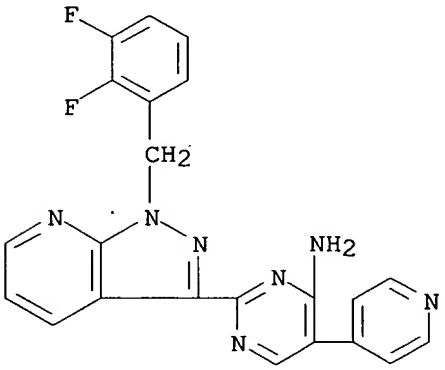
L4 ANSWER 25 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:931183 CAPLUS
DN 140:5064
TI Preparation of 2-(1-benzyl-1H-pyrazolo[3,4-b]pyridin-3-yl)-5-pyridin-4-ylpyrimidin-4-amine as guanylate cyclase stimulators
IN Weigand, Stefan; Bischoff, Erwin; Muenter, Klaus; Stasch, Johannes-peter; Stahl, Elke
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003097063	A1	20031127	WO 2003-EP4668	20030505
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10222550	A1	20031127	DE 2002-10222550	20020517
CA 2485872	AA	20031127	CA 2003-2485872	20030505
EP 1509228	A1	20050302	EP 2003-722593	20030505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI DE 2002-10222550	A	20020517		
WO 2003-EP4668	W	20030505		

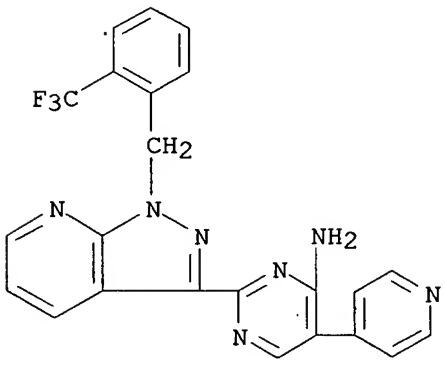
OS MARPAT 140:5064
AB Title compds. [I; R1 = Cl, F, cyano, CF3, OMe; R2 = H, F] salts, isomers, and hydrates thereof were prepd as guanylate cyclase stimulators (no data). Thus, 2-(1H-pyrazolo[3,4-b]pyridin-3-yl)-5-(4-pyridinyl)-4-pyrimidinylamine (preparation given) in DMF was stirred with Na2CO3 for 1 h at 50° followed by stirring with 2-cyanobenzyl bromide over night at 50° to give 48% 2-(3-[4-amino-5-(4-pyridinyl)-2-pyrimidinyl]-1H-pyrazolo[3,4-b]pyridin-1-yl)methylbenzonitrile.
IT **627076-58-8P 627076-59-9P 627076-60-2P**
627076-61-3P 627076-62-4P 627076-63-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (benzylpyrazolopyridinyl)pyridinylpyrimidinamine as guanylate cyclase stimulators)
RN 627076-58-8 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-chlorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 627076-59-9 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2,3-difluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)

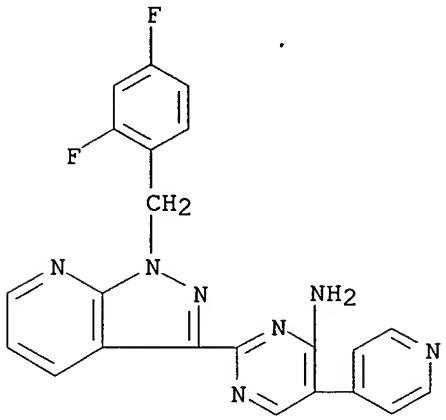


RN 627076-60-2 CAPLUS
CN 4-Pyrimidinamine, 5-(4-pyridinyl)-2-[1-[[2-(trifluoromethyl)phenyl]methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

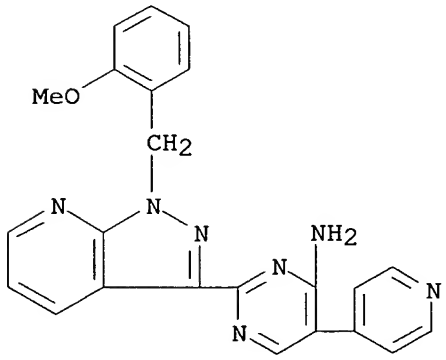


RN 627076-61-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2,4-difluorophenyl)methyl]-1H-pyrazolo[3,4-

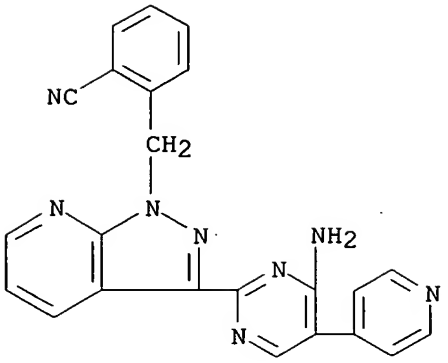
b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



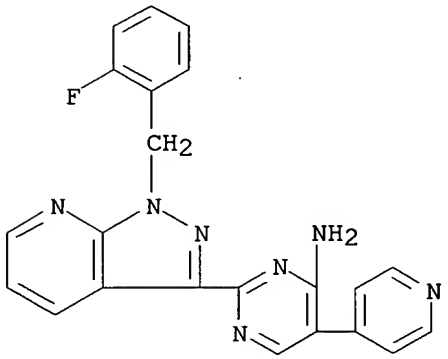
RN 627076-62-4 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-methoxyphenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 627076-63-5 CAPLUS
CN Benzonitrile, 2-[[3-[4-amino-5-(4-pyridinyl)-2-pyrimidinyl]-1H-pyrazolo[3,4-b]pyridin-1-yl]methyl]- (9CI) (CA INDEX NAME)



IT **402595-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (benzylpyrazolopyridinyl)pyridinylpyrimidinamine as guanylate cyclase stimulators)
RN 402595-29-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

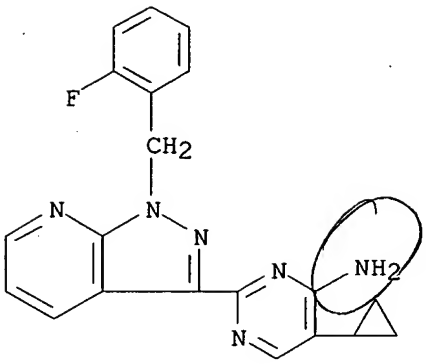
L4 ANSWER 26 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:875157 CAPLUS
DN 139:358773
TI Novel use of guanylate cyclase activators for the treatment of respiratory insufficiency
IN Grimminger, Friedrich Josef; Schermuly, Ralph; Schudt, Christian
PA Altana Pharma Ag, Germany
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003090870	A1	20031106	WO 2003-EP4243	20030424
	W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, TN, UA, US, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	EP 1356849	A1	20031029	EP 2002-9552	20020426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CA 2484089	AA	20031106	CA 2003-2484089	20030424
	EP 1501605	A1	20050202	EP 2003-722539	20030424
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005524695	T2	20050818	JP 2003-587493	20030424
	US 2005181066	A1	20050818	US 2003-512547	20030424
PRAI	EP 2002-9552	A	20020426		
	WO 2003-EP4243	W	20030424		

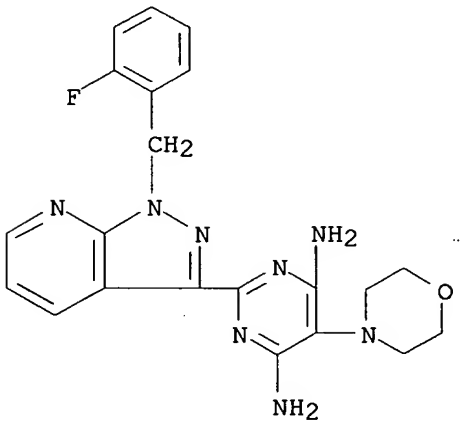
AB The invention relates to the novel use of guanylate cyclase activators for the treatment of partial and global respiratory failure. The object of the present invention is thus to provide a substance which, on oral, i.v. or else inhalational administration, leads on the one hand to the preferred dilatation of vessels in the pulmonary circulation (pulmonary selectivity) and, at the same time, to a redistribution of the blood flow within the lung in favor of the well-ventilated areas (intrapulmonary selectivity). It has now been found, surprisingly, that guanylate cyclase activators are suitable for the treatment of patients having the abovementioned mismatch. Administration of guanylate cyclase activators leads to dilatation of vessels in the pulmonary circulation and, at the same time, to a redistribution of the blood flow within the lung in favor of the well-ventilated areas. This principle, referred to hereinafter as rematching, leads to an improvement in the gas exchange function both at rest and during phys. exercise.

IT **256376-24-6**, BAY-41-2272 **256498-66-5**, BAY-41-8543
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel use of guanylate cyclase activators for treatment of respiratory insufficiency in relation to vasodilating activity and combination with other agents)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

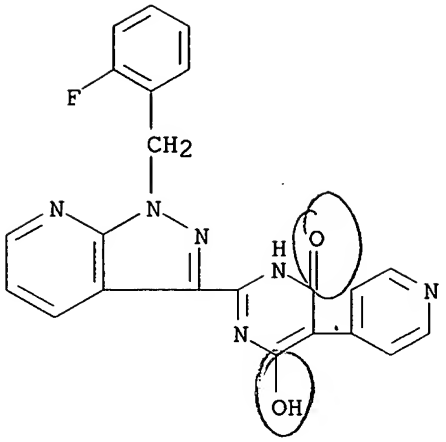


RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

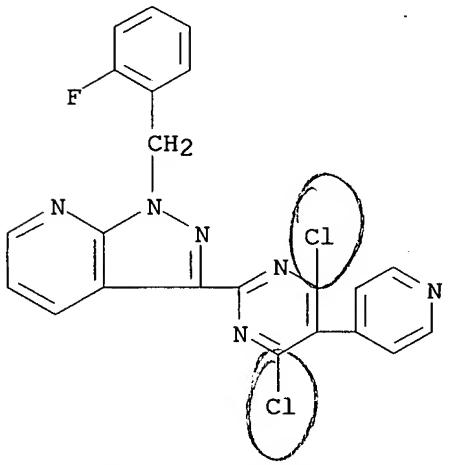
L4 ANSWER 27 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:855841 CAPLUS
DN 139:341820
TI Stents containing pyridine-substituted pyrazolopyridine derivatives for the prevention and treatment of restenosis and thrombosis
IN Feurer, Achim; Weigand, Stefan; Stelte-Ludwig, Beatrix; Grunkemeyer, Jeffry-Lynn; Low, Jeffrey; Stasch, Johannes-Peter
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003089024	A1	20031030	WO 2003-EP3950	20030416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10217799	A1	20031106	DE 2002-10217799	20020422
EP 1499369	A1	20050126	EP 2003-746828	20030416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI DE 2002-10217799	A	20020422		
WO 2003-EP3950	W	20030416		

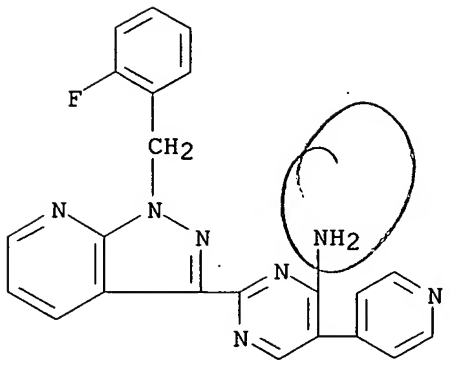
OS MARPAT 139:341820
AB The invention concerns stents containing compds. of formula (I) for the prevention and treatment of restenosis and thrombosis, especially after percutaneous transluminal coronary angioplasty; the synthesis of the compds. is described. Stents are filled or coated with one or more of the drugs.
IT **428828-70-0P 428828-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stents containing pyridine-substituted pyrazolopyridine derivs. for prevention and treatment of restenosis and thrombosis)
RN 428828-70-0 CAPLUS
CN 4(1H)-Pyrimidinone, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-6-hydroxy-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



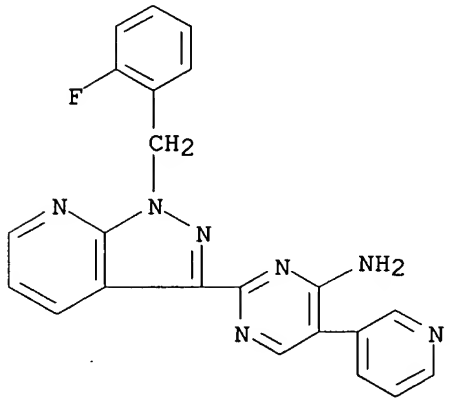
RN 428828-74-4 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[4,6-dichloro-5-(4-pyridinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



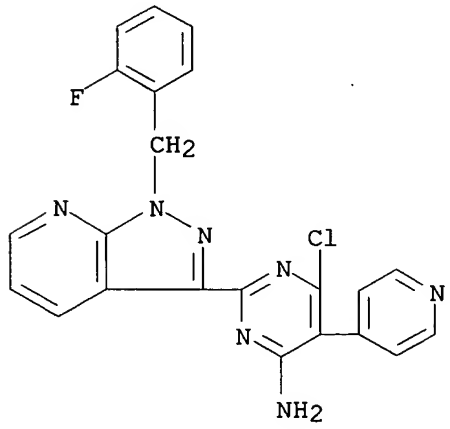
IT **402595-29-3P 428828-78-8P 428828-82-4P 428828-85-7P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stents containing pyridine-substituted pyrazolopyridine derivs. for prevention and treatment of restenosis and thrombosis)
RN 402595-29-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



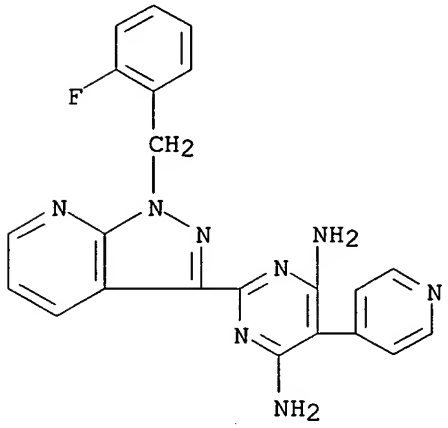
RN 428828-78-8 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 428828-82-4 CAPLUS
CN 4-Pyrimidinamine, 6-chloro-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 428828-85-7 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)

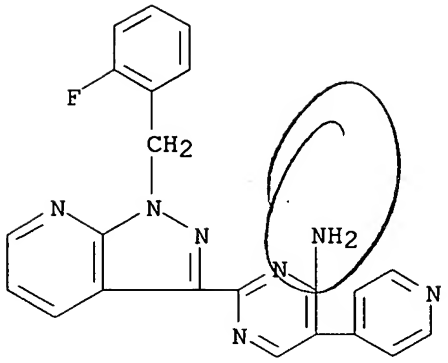


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

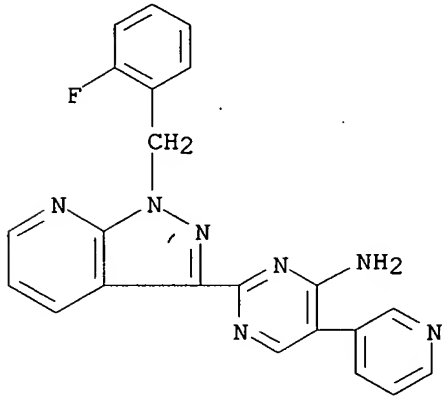
L4 ANSWER 28 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:836860 CAPLUS
DN 139:323533
TI Preparation of (pyrimidinyl)pyrazolopyridines as stimulators of soluble guanylate cyclase for treating glaucoma
IN Weigand, Stefan; Feurer, Achim; Stasch, Johannes-Peter; Huetter, Joachim
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003086407	A1	20031023	WO 2003-EP3323	20030331
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10216145	A1	20031023	DE 2002-10216145	20020412
PRAI	DE 2002-10216145	A	20020412		

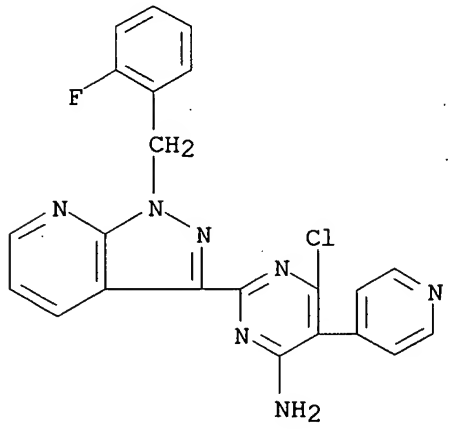
OS MARPAT 139:323533
AB Title compds. [I; R1 = 4-pyridinyl, 3-pyridinyl; R2 = H, amino, halo], were prepared as stimulators of soluble guanylate cyclase for treating glaucoma (no data). Thus, 1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxamidine (preparation given) and 4-[(dimethylamino)methylene]pyridineacetonitrile (preparation given) in xylene were reacted with BF3.OEt2 for 19 h at 140° to give 33% 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)-4-pyrimidineamine.
IT **402595-29-3P 428828-78-8P 428828-82-4P 428828-85-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (pyrimidinyl)pyrazolopyridines as stimulators of soluble guanylate cyclase for treating glaucoma)
RN 402595-29-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



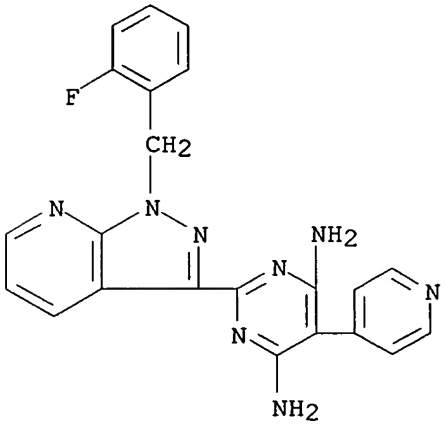
RN 428828-78-8 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(3-pyridinyl)- (9CI) (CA INDEX NAME)



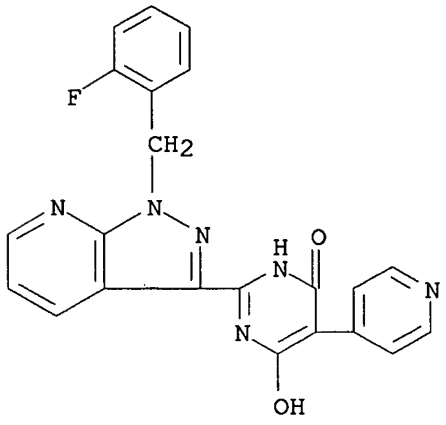
RN 428828-82-4 CAPLUS
CN 4-Pyrimidinamine, 6-chloro-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



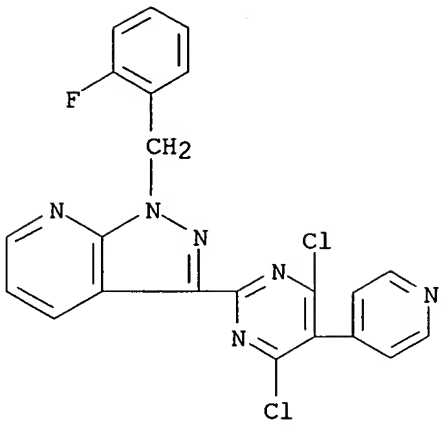
RN 428828-85-7 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



IT **428828-70-0P 428828-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (pyrimidinyl)pyrazolopyridines as stimulators of soluble guanylate cyclase for treating glaucoma)
RN 428828-70-0 CAPLUS
CN 4(1H)-Pyrimidinone, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-6-hydroxy-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)

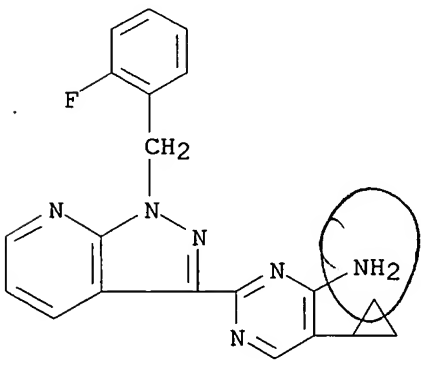


RN 428828-74-4 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[4,6-dichloro-5-(4-pyridinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



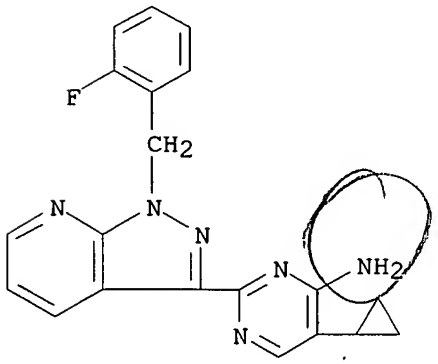
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:770805 CAPLUS
DN 140:104877
TI Relaxing effects induced by the soluble guanylyl cyclase stimulator BAY 41-2272 in human and rabbit corpus cavernosum
AU Baracat, Juliana S.; Teixeira, Cleber E.; Okuyama, Cristina E.; Priviero, Fernanda B. M.; Faro, Renato; Antunes, Edson; De Nucci, Gilberto
CS UNICAMP, Department of Pharmacology, Faculty of Medical Sciences, Campinas, 13081-970, Brazil
SO European Journal of Pharmacology (2003), 477(2), 163-169
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB 5-Cyclopropyl-2-[1-(2-fluoro-benzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-pyrimidin-4-ylamine (BAY 41-2272) is a potent soluble guanylyl cyclase stimulator in a nitric oxide (NO)-independent manner. The relaxant effect of BAY 41-2272 was investigated in rabbit and human corpus cavernosum in vitro. BAY 41-2272 (0.01-10 μM) relaxed both rabbit (pEC50=6.82±0.06) and human (pEC50=6.12±0.10) precontracted cavernosal strips. The guanylyl cyclase inhibitor (ODQ, 10 μM) caused significant rightward shifts in the concentration-response curves for BAY 41-2272 in rabbit (4.7-fold) and human (2.3-fold) tissues. The NO synthesis inhibitor (N-nitro-l-arginine Me ester (l-NAME), 100 μM) also produced similar rightward shifts, revealing that BAY 41-2272 acts synergistically with endogenous NO to elicit its relaxant effect. The results also indicate that ODQ is selective for the NO-stimulated enzyme, since relaxations evoked by BAY 41-2272 were only partly attenuated by ODQ. The present study shows that both BAY 41-2272 and sildenafil evoke relaxations independent of inhibition of haem in soluble guanylate cyclase. Moreover, there is no synergistic effect of the two compds. in corpus cavernosum.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); BIOL (Biological study)
(relaxing effects induced by the soluble guanylyl cyclase stimulator BAY 41-2272 in human and rabbit corpus cavernosum)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

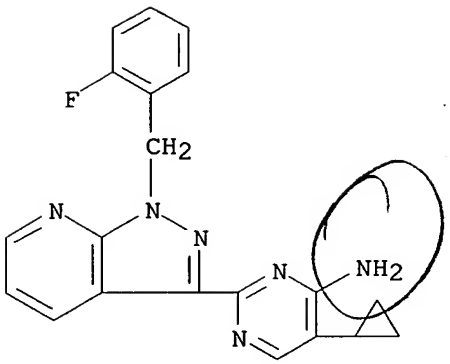


RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:725321 CAPLUS
DN 140:174791
TI Antiplatelet properties of a novel, non-NO-based soluble guanylate cyclase activator, BAY 41-2272
AU Hobbs, Adrian J.; Moncada, Salvador
CS Cruciform Building, Wolfson Institute for Biomedical Research, University College London, London, WC1E 6AE, UK
SO Vascular Pharmacology (2003), 40(3), 149-154
CODEN: VPAHAJ; ISSN: 1537-1891
PB Elsevier Science B.V.
DT Journal
LA English
AB Nitric oxide (NO) plays an important role in cardiovascular homeostasis, particularly in the regulation of vascular tone and the reactivity of platelets and circulating cells. Soluble guanylate cyclase (sGC) acts as the principal biol. target for NO and catalyzes the formation of the intracellular second messenger cyclic GMP (cGMP); activation of this enzyme is thought to be responsible for the majority of cardiovascular actions of NO. In the present study, the authors have evaluated the antiplatelet effects of a novel non-NO-based sGC activator, BAY 41-2272, in vitro and in vivo. BAY 41-2272 produced a marked inhibition of platelet aggregation in washed platelets with a potency (IC50 .apprx.100 nM) some 3-fold less than the NO donor S-nitrosoglutathione. BAY 41-2272 also prevented aggregation in platelet-rich plasma (PRP), albeit with a much lower potency. Both NO and prostacyclin exhibited synergistic activity with BAY 41-2272 to inhibit platelet aggregation. In vivo, at doses of BAY 41-2272 that significantly reduced blood pressure, the compound had little effect on FeCl3-induced thrombosis. These data confirm that intraplatelet sGC activation results in inhibition of aggregation and suggests that novel non-NO-based sGC activators, which possess both hypotensive and antiplatelet activities, may be useful as therapeutic agents.
IT **256376-24-6**, BAY 41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiplatelet properties of non-NO-based soluble guanylate cyclase activator BAY 41-2272)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

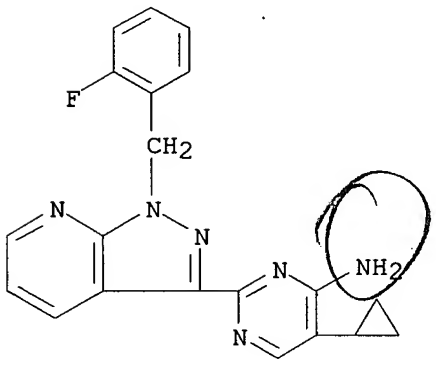


L4 ANSWER 31 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:638740 CAPLUS
DN 139:272820
TI A constitutively activated mutant of human soluble guanylyl cyclase (sGC): Implication for the mechanism of sGC activation
AU Martin, Emil; Sharina, Iraida; Kots, Alexander; Murad, Ferid
CS Department of Integrative Biology and Pharmacology and Institute of Molecular Medicine, University of Texas Health Science Center, Houston, TX, 77030, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(16), 9208-9213
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Heterodimeric αβ soluble guanylyl cyclase (sGC) is a recognized receptor for nitric oxide (NO) and mediates many of its physiol. functions. Although it has been clear that the heme moiety coordinated by His-105 of the β subunit is crucial for mediating the activation of the enzyme by NO, it is not understood whether the heme moiety plays any role in the function of the enzyme in the absence of NO. Here we analyze the effects of biochem. and genetic removal of heme and its reconstitution on the activity of the enzyme. Detergent-induced loss of heme from the wild-type αβ enzyme resulted in several-fold activation of the enzyme. This activation was inhibited after hemin reconstitution. A heme-deficient mutant αβCys-105 with Cys substituted for His-105 was constitutively active with specific activity approaching the activity of the wild-type enzyme activated by NO. However, reconstitution of mutant enzyme with heme and/or DTT treatment significantly inhibited the enzyme. Mutant enzyme reconstituted with ferrous heme was activated by NO and CO alone and showed additive effects between gaseous effectors and the allosteric activator 5-cyclopropyl-2-[1-(2-fluoro-benzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-yrimidin-4-ylamine. We propose that the heme moiety through its coordination with His-105 of the β subunit acts as an endogenous inhibitor of sGC. Disruption of the heme-coordinating bond induced by binding of NO releases the restrictions imposed by this bond and allows the formation of an optimally organized catalytic center in the heterodimer.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heme prosthetic group of soluble guanylyl cyclase maintains enzyme basal state with regulatory domain in inhibited restricted conformation through coordination with axial His105 residue)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



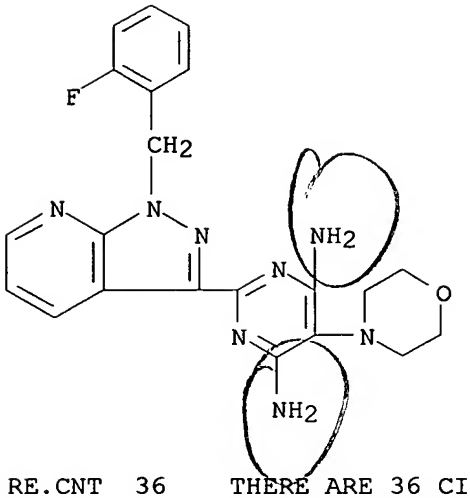
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:638592 CAPLUS
DN 140:86777
TI Soluble guanylyl cyclase: Physiological role as an NO receptor and the potential molecular target for therapeutic application
AU Nakane, Masaki
CS Neuroscience Research, Global Pharmaceutical Research & Development, Abbott Laboratories, Abbott Park, IL, USA
SO Clinical Chemistry and Laboratory Medicine (2003), 41(7), 865-870
CODEN: CCLMFW; ISSN: 1434-6621
PB Walter de Gruyter GmbH & Co. KG
DT Journal; General Review
LA English
AB A review and discussion. NO activates soluble guanylyl cyclase (sGC), which results in an increased biosynthesis of cGMP, and smooth muscle relaxation and vasodilation. The heme group in sGC binds NO and allosterically activates the catalytic site. In addition, a 2nd allosteric site that synergistically activates the enzyme has been reported. BAY 41-2272 has been reported as an NO-independent activator of sGC. Treatment with this compound results in anti-platelet activity, a decrease in blood pressure, and an increase in survival, indicating a potential for treating cardiovascular diseases. YC-1, another NO-independent activator, activates sGC and the activity is enhanced in the presence of NO. YC-1 relaxes tissue strips in an organ bath. Consistent with its biochem. activity, YC-1 has induced penile erection in a conscious rat model. Recently, the authors found a novel series of sGC activators (A-344905, A-350619) that also NO-independently activate sGC and cause penile erection, suggesting a synergy with endogenous NO production in vivo. Here, the author reviews the NO/cGMP signal transduction pathway and defines sGC modulators as a novel approach for the treatment of cardiovascular diseases and erectile dysfunction.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(physiol. role of soluble guanylyl cyclase as a nitric oxide receptor and a potential mol. target for therapeutic application)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:365029 CAPLUS
DN 139:193424
TI Mechanisms of nitric oxide independent activation of soluble guanylyl cyclase
AU Schmidt, Peter; Schramm, Matthias; Schroder, Henning; Stasch, Johannes-Peter
CS Institute of Cardiovascular Research, Bayer AG, Wuppertal, D-42096, Germany
SO European Journal of Pharmacology (2003), 468(3), 167-174
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB The heterodimeric heme-protein soluble guanylyl cyclase (sGC) is the only proven receptor for nitric oxide (NO). Recently, two different types of NO-independent soluble guanylyl cyclase stimulators have been discovered. The heme-dependent stimulator BAY 41-8543 stimulates the enzyme in a synergistic fashion when combined with NO, requires the presence of the heme group and can be blocked by the soluble guanylyl cyclase inhibitor 1H-(1,2,4)-Oxadiazole-(4,3-a)-quinoxalin-1-one (ODQ). The heme-independent activator BAY 58-2667 activates soluble guanylyl cyclase even in the presence of ODQ or rendered heme-deficient. In the present study, BAY 41-8543, BAY 58-2667 and NO strongly increased Vmax. Combination of BAY 58-2667 and NO increased Vmax in an additive manner, whereas the synergistic effect of BAY 41-8543 and NO on enzyme activation was reflected in an overadditive increase of Vmax. ODQ potentiated Vmax of BAY 58-2667-stimulated soluble guanylyl cyclase. BAY 41-8543 prolonged the half-life of the nitrosyl-heme complex of NO-activated enzyme, an effect that was not observed with BAY 58-2667. These results show the different activation patterns of both compds. and demonstrate their value as tools to investigate the mechanisms that underlie soluble guanylyl cyclase activation.
IT **256498-66-5**, BAY 41-8543
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(mechanisms of nitric oxide independent activation of soluble guanylyl cyclase)
RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

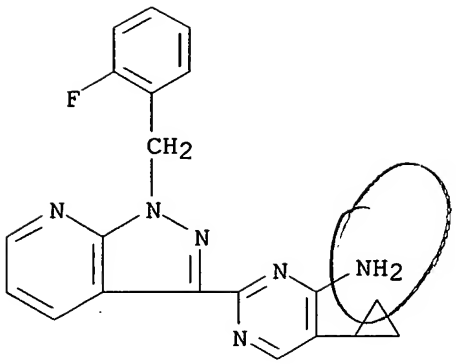
L4 ANSWER 34 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:202525 CAPLUS
DN 138:243276
TI Vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate
IN Wnendt, Stephan; Chaplin, David; Kuttler, Bernd; Lorenz, Guenter
PA Oxygene Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003020331	A1	20030313	WO 2002-EP9836	20020903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10142897	A1	20030320	DE 2001-10142897	20010903
DE 10142881	A1	20030403	DE 2001-10142881	20010903
US 2005065595	A1	20050324	US 2004-488515	20041021
PRAI DE 2001-10142881	A	20010903		
DE 2001-10142897	A	20010903		
WO 2002-EP9836	W	20020903		

AB The invention relates to implants, in particular intracavernous or intravascular implants, preferably for the treatment or prophylaxis of coronary or peripheral vascular occlusion, strictures or stenosis, in particular for the prophylaxis of restenosis. The implants contain combretastatin A-4 or combretastatin A-4 phosphate that is chemical bonded in a covalent or non-covalent form or is in a phys. fixed form. Stents prepared from alloys, polymers or their combination, also with alumina coating are treated with the alc. solution of combretastatin A-4 or combretastatin A-4 phosphate under sterile condition. According to an other method combretastatin A-4 or combretastatin A-4 phosphate are included in a biodegradable polymer for coating. Other drugs can be added to the implants.

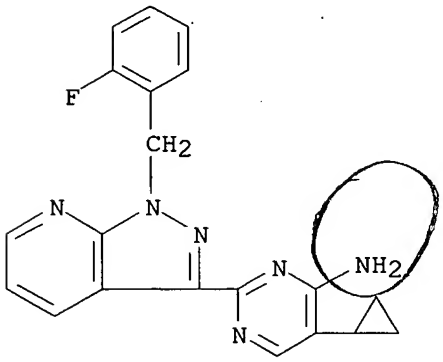
IT **256376-24-6**, BAY 41-2272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



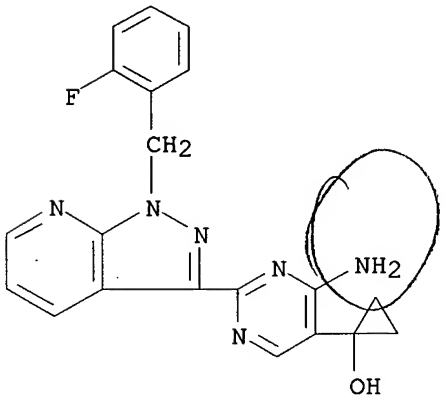
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:130131 CAPLUS
DN 139:63276
TI The Rho-kinase inhibitor Y-27632 and the soluble guanylyl cyclase activator BAY41-2272 relax rabbit vaginal wall and clitoral corpus cavernosum
AU Cellek, Selim
CS Wolfson Institute for Biomedical Research, University College London, London, WC1E 6BT, UK
SO British Journal of Pharmacology (2003), 138(2), 287-290
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB The effects of Y-27632, a Rho-kinase inhibitor and BAY41-2272, a soluble guanylyl cyclase activator, on the tone and nitrergic responses of rabbit vaginal wall and clitoral corpus cavernosum were investigated. Y-27632 and BAY41-2272 (10 nM-10 μM) elicited concentration-dependent relaxation of phenylephrine-induced tone in both tissues. IC50 values of Y-27632 for vaginal and clitoral tissues were 370±30 nM, and 467±14 nM, resp. BAY41-2272 had IC50 values of 478±54 nM and 304±38 nM resp. The effect of the Y-27632 on the tissue tone was not affected by an inhibitor of nitric oxide synthase (L-NAME; 500 μM). However, L-NAME reduced the potency of BAY41-2272 in the clitoral corpus cavernosum but not in the vaginal wall. BAY41-2272 enhanced nitrergic relaxation responses only in the clitoral corpus cavernosum. Y-27632 had no effect on nitrergic relaxations in either tissue. These results demonstrate that Y-27632 and BAY41-2272 elicit relaxation of the rabbit vaginal wall and clitoral corpus cavernosum.
IT **256376-24-6**, BAY41-2272
RL: PAC (Pharmacological activity); BIOL (Biological study)
(Rho-kinase inhibitor Y-27632 and the soluble guanylyl cyclase activator BAY41-2272 relax rabbit vaginal wall and clitoral corpus cavernosum)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

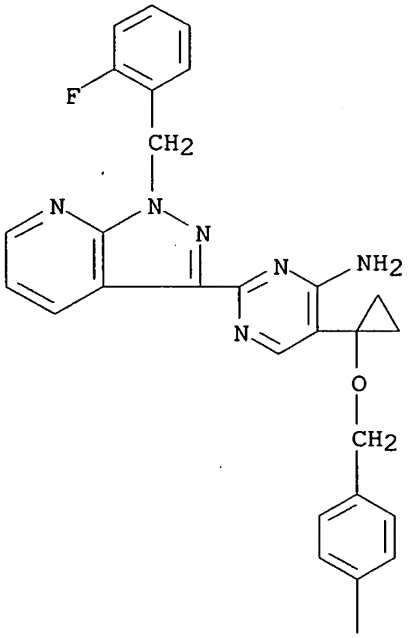
L4 ANSWER 36 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:109219 CAPLUS
DN 139:36499
TI Cyclopropyl building blocks in organic synthesis. 84. A new and productive route to 1-heteroarylcyclopropanols
AU Belov, Vladimir N.; Savchenko, Andrei I.; Sokolov, Viktor V.; Straub, Alexander; de Meijere, Armin
CS Institut fur Organische Chemie, Georg-August-Universitat Gottingen, Gottingen, 37077, Germany
SO European Journal of Organic Chemistry (2003), (3), 551-561
CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 139:36499
AB Methoxy[(alkoxy)cyclopropyl]propenenitrile derivs. were designed and prepared from Et cyclopropylidenacetate as a valuable precursor to various 1-heteroarylcyclopropanols. The key intermediates in this study included 3-methoxy-2-[1-[(4-methoxyphenyl)methoxy]cyclopropyl]-2-propenenitrile and 3-methoxy-2-[1-[(2-propenyl)oxy]cyclopropyl]-2-propenenitrile (I). Condensation of I with amidines, guanidine, hydrazine, and Me thioglycolate and subsequent removal of the allyl protecting group yields 1-heteroarylcyclopropanols such as 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]cyclopropanol (BAY 41-2272 metabolite II). II is a known very potent NO-independent stimulator of soluble guanylate cyclase. Direct cleavage of the allyl ether protecting group by palladium-catalyzed substitution with lithium p-toluenesulfinate in AcOH or treatment with cyclohexylmagnesium bromide/Ti(OiPr)4 gives highly functionalized, sterically congested 1-heteroarylcyclopropanols with intact amino and ester groups.
IT **304874-04-2P**, 1-[4-Amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]cyclopropanol
RL: SPN (Synthetic preparation); PREP (Preparation)
(BAY 41-2272 metabolite; preparation of [(amino)pyrimidinyl]cyclopropanol derivs. and analogs from methoxy[(alkoxy)cyclopropyl]propenenitrile derivs. as key intermediates)
RN 304874-04-2 CAPLUS
CN Cyclopropanol, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



IT **540134-07-4P 540134-11-0P 540134-27-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(amino)pyrimidinyl]cyclopropanol derivs. and analogs from methoxy[(alkoxy)cyclopropyl]propenenitrile derivs. as key intermediates)

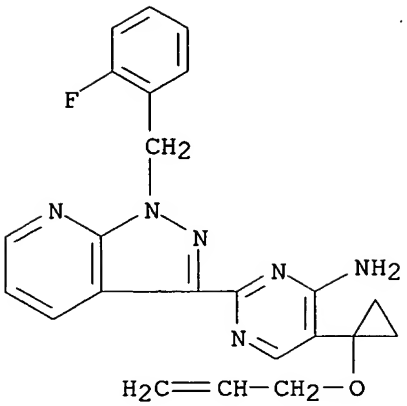
RN 540134-07-4 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-[1-[(4-methoxyphenyl)methoxy]cyclopropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



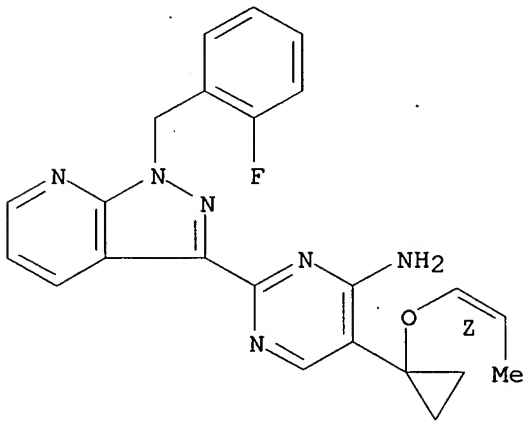
PAGE 2-A

RN 540134-11-0 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-[1-(2-propenyloxy)cyclopropyl]- (9CI) (CA INDEX NAME)

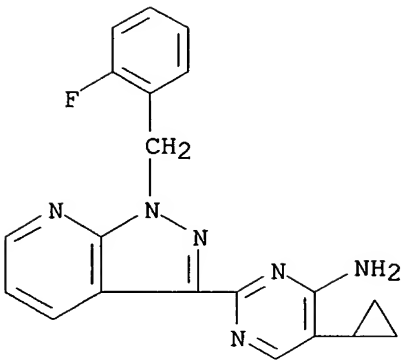


RN 540134-27-8 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-[1-[(1Z)-1-propenyloxy]cyclopropyl]- (9CI) (CA INDEX NAME)

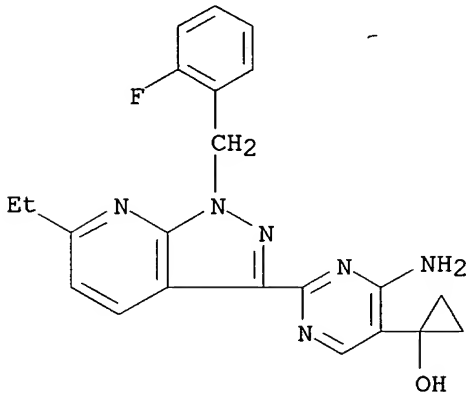
Double bond geometry as shown.



IT **256376-24-6DP**, BAY 41-2272, metabolite **540134-31-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [(amino)pyrimidinyl]cyclopropanol derivs. and analogs from methoxy[(alkoxy)cyclopropyl]propenenitrile derivs. as key intermediates)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

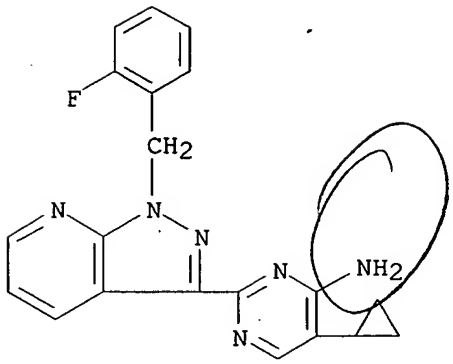


RN 540134-31-4 CAPLUS
CN Cyclopropanol, 1-[4-amino-2-[6-ethyl-1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



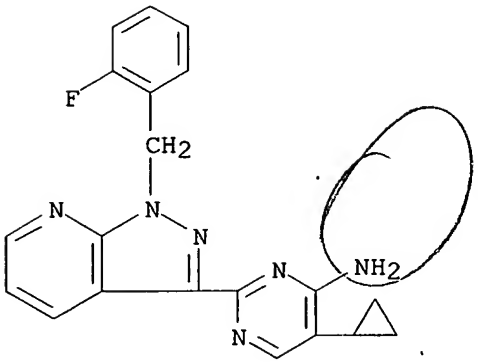
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:82913 CAPLUS
DN 139:255018
TI Cardiorenal and Humoral Properties of a Novel Direct Soluble Guanylate Cyclase Stimulator BAY 41-2272 in Experimental Congestive Heart Failure
AU Boerrigter, Guido; Costello-Boerrigter, Lisa C.; Cataliotti, Alessandro; Tsuruda, Toshihiro; Harty, Gail J.; Lapp, Harald; Stasch, Johannes-Peter; Burnett, John C.
CS Cardiorenal Research Laboratory, Mayo Clinic and Foundation, Rochester, MN, 55905, USA
SO Circulation (2003), 107(5), 686-689
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB BAY 41-2272 is a recently introduced novel orally available agent that directly stimulates soluble guanylate cyclase (sGC) and sensitizes it to its physiol. stimulator, nitric oxide. To date, its therapeutic actions in congestive heart failure (CHF) remain undefined. We characterized the cardiorenal actions of i.v. BAY 41-2272 in a canine model of CHF and compared it to nitroglycerin (NTG). CHF was induced by rapid ventricular pacing for 10 days. Cardiorenal and humoral function were assessed at baseline and with administration of 2 doses of BAY 41-2272 (2 and 10 μg · kg-1 · min-1; n=8) or NTG (1 and 5 μg · kg-1 · min-1; n=6). Administration of 10 μg · kg-1 · min-1 BAY 41-2272 reduced mean arterial pressure (113±8 to 94±6 mm Hg; P<0.05), pulmonary artery pressure (29±2 to 25±2 mm Hg; P<0.05), and pulmonary capillary wedge pressure (25±2 to 20±2 mm Hg; P<0.05). Cardiac output (2.1±0.2 to 2.3±0.2 L/min; P<0.05) and renal blood flow (131±17 to 162±18 mL/min; P<0.05) increased. Glomerular filtration rate was maintained. There were no changes in plasma renin activity, angiotensin II, or aldosterone. NTG mediated similar hemodynamic changes and addnl. decreased right atrial pressure and pulmonary vascular resistance. The new sGC stimulator BAY 41-2272 potently unloaded the heart, increased cardiac output, and preserved glomerular filtration rate without activation of the renin-angiotensin-aldosterone system in exptl. CHF. These beneficial properties make direct sGC stimulation with BAY 41-2272 a promising new strategy for the treatment of cardiovascular diseases such as CHF.
IT **256376-24-6**, BAY 41-2272
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cardiorenal and humoral properties of guanylate cyclase stimulator BAY 41-2272 compared to nitroglycerin in congestive heart failure)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



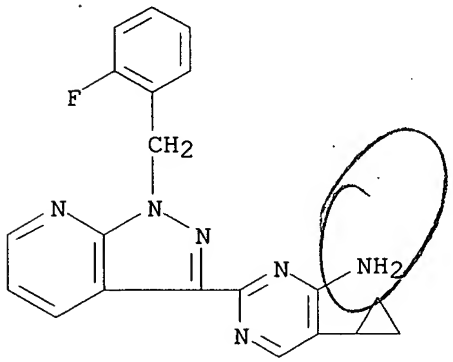
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:63984 CAPLUS
DN 139:224044
TI BAY41-2272, a novel nitric oxide independent soluble guanylate cyclase activator, relaxes human and rabbit corpus cavernosum in vitro
AU Kalsi, Jas S.; Rees, Rowland W.; Hobbs, Adrian J.; Royle, Michael; Kell, Phil D.; Ralph, David J.; Moncada, Salvador; Cellek, Selim
CS Wolfson Institute for Biomedical Research and Institute of Urology, Middlesex Hospital, University College London, UK
SO Journal of Urology (Hagerstown, MD, United States) (2003), 169(2), 761-766
CODEN: JOURAA; ISSN: 0022-5347
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB In cavernous smooth muscle nitric oxide (NO) activates soluble guanylate cyclase, which catalyzes the synthesis of cyclic guanosine 3',5'-monophosphate, leading to smooth muscle relaxation, increased blood flow and penile erection. The pyrazolopyridine derivative BAY41-2272 (5-cyclopropyl-2-[1-(2-fluoro-benzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]pyrimidin-4ylamine) was identified and found to stimulate soluble guanylate cyclase in a NO independent manner. We investigated the effect of BAY41-2272 on human and rabbit corpus cavernosum. We investigated the effect of BAY41-2272 on the tone and nitrergic relaxation responses of human and rabbit cavernous strips in the absence and presence of the soluble guanylate cyclase inhibitor ODQ (1H-[1,2,4]oxadiazolo[4-3a]quinoxalin-1-one) or the NO synthase inhibitor L-NAME (N-nitro-L-arginine-Me ester HCl). The potency of BAY41-2272 was compared to that of another soluble guanylate cyclase activator YC-1, and the NO releasing compound spermine NONOate (N-2-aminoethyl-N-2-hydroxy-2-nitrosohydroazino-1,2-ethylenediamine). BAY41-2272 resulted in concentration dependent relaxation of human and rabbit cavernosum (mean EC50 ± SEM 489.1 ± 22.5 and 406.3 ± 21.5 nM., resp.). The compound was 32 times more potent than YC-1 and twice as potent as spermine-NONOate. ODQ decreased the potency of BAY41-2272, such that in the presence of 30 μM. ODQ the EC50 of BAY41-2272 induced relaxation was 1,407.3 ± 158.0 and 1,902.7 ± 11.0 nM. in human and rabbit tissues, resp. L-NAME also inhibited relaxations elicited by BAY41-2272 in rabbit tissue. In the presence of 500 μM. L-NAME the EC50 of BAY41-2272 induced responses was 836.7 ± 46.7 nM. BAY41-2272 at subthreshold concns. of 30 to 50 nM. potentiated nitrergic responses. Moreover, the inhibition of nitrergic responses by L-NAME was reversed by 0.3 to 3 μM. BAY41-2272. We report that a nonNO based soluble guanylate cyclase activator relaxes human and rabbit corpus cavernosum, and potentiates nitrergic responses.
IT **256376-24-6**, BAY41-2272
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of BAY41-2272, nitric oxide independent soluble guanylate cyclase activator, on human and rabbit corpus cavernosum)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

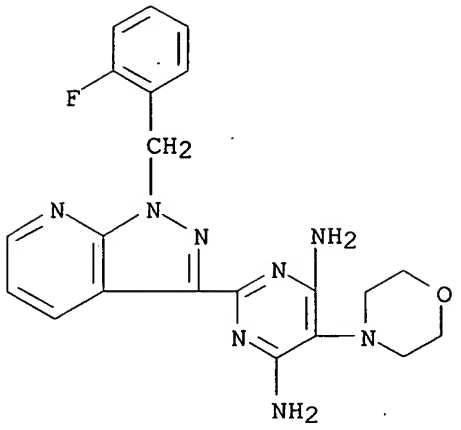


RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:52520 CAPLUS
DN 139:16962
TI Drugs that activate specific nitric oxide sensitive guanylyl cyclase isoforms independent of nitric oxide release
AU Behrends, Sonke
CS Institute of Experimental and Clinical Pharmacology and Toxicology, University clinic Hamburg-Eppendorf, Hamburg, D-20246, Germany
SO Current Medicinal Chemistry (2003), 10(4), 291-301
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review. Nitric oxide (NO) releasing drugs have helped patients suffering from angina pectoris for more than a century. In the 1970s NO-sensitive guanylyl cyclase was identified as the target of NO. Since then, three different isoforms of the enzyme have been identified. All NO-releasing drugs act by binding of NO to the prosthetic heme group common to all three isoforms. They thus act all as isoform-unspecific substances. This review addresses recently developed drugs that activate NO-sensitive guanylyl cyclase independent of NO-release. They have great potential in the treatment of angina pectoris, hypertension and erectile dysfunction. The mol. target has been validated by the successful clin. use of NO-releasing drugs for more than a century. At the same time the mode of action of these drugs is entirely new. The development of highly isoform-specific derivs. with distinct pharmacol. profiles is now an open possibility with great potential.
IT **256376-24-6**, BAY 41-2272 **256498-66-5**, BAY 41-8543
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drugs that activate specific nitric oxide sensitive guanylyl cyclase isoforms)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RE.CNT 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:42280 CAPLUS
DN 138:106723
TI Preparation of morpholine-bridged pyrazolopyridine derivatives as stimulators for soluble guanylate cyclase
IN Feurer, Achim; Flubacher, Dietmar; Weigand, Stefan; Stasch, Johannes-Peter; Stahl, Elke; Schenke, Thomas; Alonso-Alija, Cristina; Wunder, Frank; Lang, Dieter; Dembowsky, Klaus; Straub, Alexander; Perzborn, Elisabeth
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

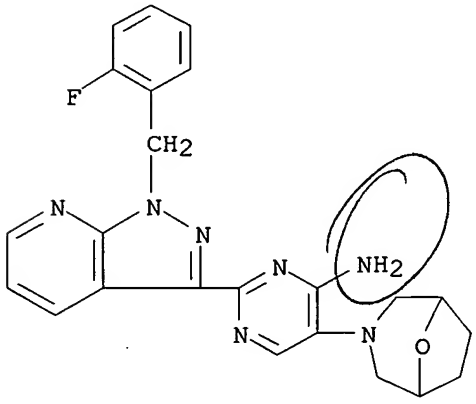
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003004503	A1	20030116	WO 2002-EP6991	20020625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10132416	A1	20030116	DE 2001-10132416	20010704
CA 2452590	AA	20030116	CA 2002-2452590	20020625
EP 1406908	A1	20040414	EP 2002-745409	20020625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501034	T2	20050113	JP 2003-510670	20020625
US 2004235863	A1	20041125	US 2004-482766	20040628
PRAI DE 2001-10132416	A	20010704		
WO 2002-EP6991	W	20020625		

OS CASREACT 138:106723; MARPAT 138:106723
AB The invention relates to novel pyrazolopyridine derivs. I [R1 = Ra, Rb; X = (CH2)n; n = 1, 2; R2 = H, NH2] and to salts, isomers and hydrates thereof as stimulators for soluble guanylate cyclase and to their use as agents in the treatment of cardiovascular diseases, hypertonicity, thromboembolic diseases and ischemia, sexual dysfunction or inflammations and for the treatment of diseases of the central nervous system. The invention also relates to the preparation of I through heating in an organic solution with pyrazolopyridine II with nitriles, Alk-CO2CH:CR1CN (Alk = C1-4-alkyl); or with malonates, R1CH(CO2Et)2, to give pyrimidine III; halogenation of the latter to give pyrimidine IV (R2 = halogen); then, heating of IV (R2 = halogen) with aqueous NH3 to give IV (R2 = NH2). Thus, I (R1 = Ra, X = CH2; R2 = H) was prepared in 16% from II·HCl via heating with AcOCH:CRaCN (X = CH2) in PhMe. Pyrazolopyridine I (R1 = Ra, X = CH2; R2 = H) was tested for vascular relaxing activity [IC50 = 0.27 μM].
IT **485812-73-5P 485812-74-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and pharmaceutical activity of; preparation of morpholine-bridged
pyrazolopyridine derivs. as stimulators for soluble guanylate cyclase)

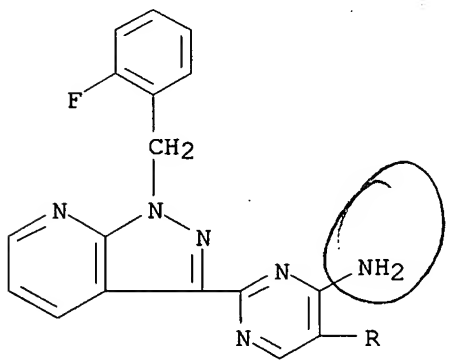
RN 485812-73-5 CAPLUS

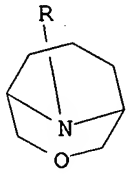
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- (9CI) (CA INDEX NAME)



RN 485812-74-6 CAPLUS

CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)- (9CI) (CA INDEX NAME)



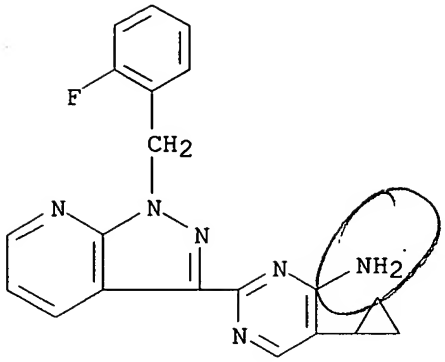


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:942701 CAPLUS
DN 138:8413
TI Vascular implants treated with FK506
IN Wnendt, Stephan; Von Oepen, Randolf; Kuttler, Bernd; Lang, Gerhard
PA Jomed G.m.b.H., Germany
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10127330	A1	20021212	DE 2001-10127330	20010606
	WO 2002065947	A2	20020829	WO 2002-EP1707	20020218
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1372753	A2	20040102	EP 2002-700248	20020218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004531299	T2	20041014	JP 2002-565512	20020218
	CN 1547490	A	20041117	CN 2002-805091	20020218
PRAI	DE 2001-10107339	A	20010216		
	DE 2001-10127011	A	20010605		
	DE 2001-10127330	A	20010606		
	WO 2002-EP1707	W	20020218		

AB The invention concerns vascular implants that include a metal, or an alloy base, a ceramic or polymer coating and covalently bound or phys. immobilized FK506 for the treatment of stenosis and restenosis. In addition, the implants can include other drugs. For the preparation, the coated implant is incubated with a solution of FK506; or FK506 is added during polymerization coating.
IT **256376-24-6**, BAY 41-2272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants treated with FK506)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)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CH2
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NH2
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L4 ANSWER 42 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:941572 CAPLUS
DN 138:8411
TI Vascular implants treated with FK506
IN Wnendt, Stephan; Von Oepen, Randolf; Kuttler, Bernd; Lang, Gerhard
PA Jomed G.m.b.H., Germany
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10127011	A1	20021212	DE 2001-10127011	20010605
	DE 10107339	A1	20020905	DE 2001-10107339	20010216
	WO 2002065947	A2	20020829	WO 2002-EP1707	20020218
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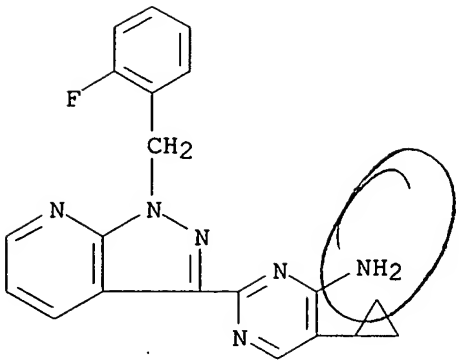
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1372753	A2	20040102	EP 2002-700248	20020218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004531299	T2	20041014	JP 2002-565512	20020218
	CN 1547490	A	20041117	CN 2002-805091	20020218
PRAI	DE 2001-10107339	A	20010216		
	DE 2001-10127011	A	20010605		
	DE 2001-10127330	A	20010606		
	WO 2002-EP1707	W	20020218		

AB The invention concerns vascular implants that include a metal, or an alloy base, a ceramic or polymer coating and covalently bound or phys. immobilized FK506 for the treatment of stenosis and restenosis. In addition, the implants can include other drugs. For the preparation, the coated implant is incubated with a solution of FK506; or FK506 is added during polymerization coating.

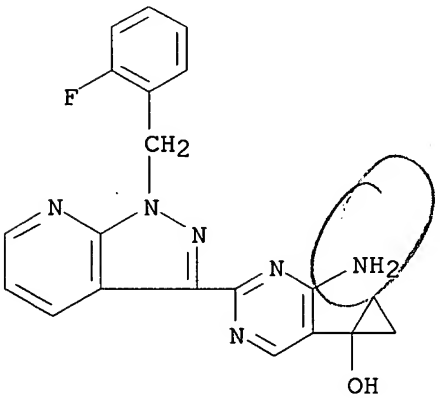
IT **256376-24-6**, BAY 41-2272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants treated with FK506)

RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

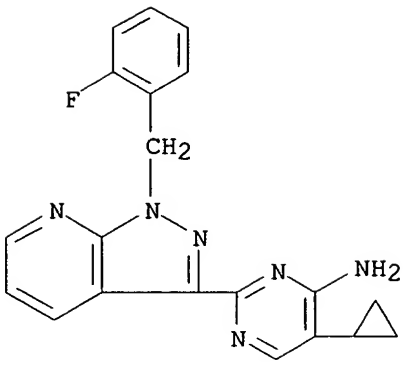


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

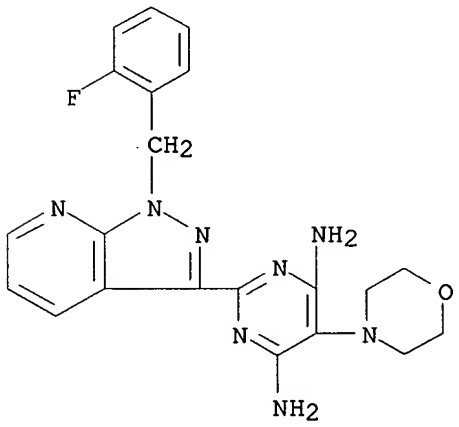
L4 ANSWER 43 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:512251 CAPLUS
DN 139:190571
TI Metabolites of orally active NO-independent pyrazolopyridine stimulators of soluble guanylate cyclase. [Erratum to document cited in CA137:226160]
AU Straub, Alexander; Benet-Buchholz, Jordi; Frode, Rita; Kern, Armin; Kohlsdorfer, Christian; Schmitt, Peter; Schwarz, Thomas; Siefert, Hans-Martin; Stasch, Johannes-Peter
CS Institute of Medicinal Chemistry, Bayer AG, Pharma Research Centre, Wuppertal, D-42096, Germany
SO Bioorganic & Medicinal Chemistry (2002), 10(9), 3075
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB On page 1711 and in the graphical abstract the second author's name should read Jordi Benet-Buchholz instead of Jordi Benet-Buckholz.
IT **304874-04-2P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of orally active NO-independent pyrazolopyridine stimulators of soluble guanylate cyclase (Erratum))
RN 304874-04-2 CAPLUS
CN Cyclopropanol, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



IT **256376-24-6**, BAY 41-2272 **256498-66-5**, BAY 41-8543
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of orally active NO-independent pyrazolopyridine stimulators of soluble guanylate cyclase (Erratum))
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 44 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:391319 CAPLUS
DN 136:401774
TI Preparation of pyridinylpyrimidine-substituted pyrazolopyridines as inhibitors of cGMP degradation
IN Stasch, Johannes-Peter; Feurer, Achim; Weigand, Stefan; Stahl, Elke; Flubacher, Dietmar; Alonso-Alija, Cristina; Wunder, Frank; Lang, Dieter; Dembowsky, Klaus; Straub, Alexander; Perzborn, Elisabeth
PA Bayer AG, Germany
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10131987	A1	20020523	DE 2001-10131987	20010702
	US 2002173514	A1	20021121	US 2001-1569	20011101
	US 6693102	B2	20040217		
	CA 2429312	AA	20020530	CA 2001-2429312	20011109
	WO 2002042301	A1	20020530	WO 2001-EP12969	20011109
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002020692	A5	20020603	AU 2002-20692	20011109
	BR 2001015477	A	20030819	BR 2001-15477	20011109
	EP 1343786	A1	20030917	EP 2001-997489	20011109
	EP 1343786	B1	20050629		
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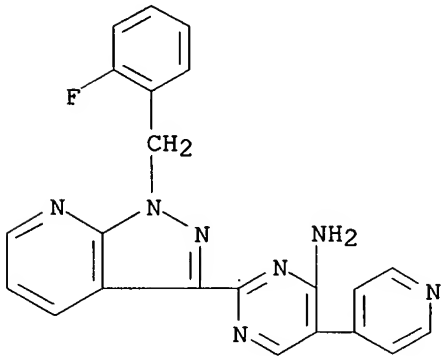
	EE 200300243	A	20031015	EE 2003-243	20011109
	JP 2004521872	T2	20040722	JP 2002-544435	20011109
	CN 1555374	A	20041215	CN 2001-822206	20011109
	CZ 294648	B6	20050216	CZ 2003-1435	20011109
	AT 298752	E	20050715	AT 2001-997489	20011109
	TW 582998	B	20040411	TW 2001-90128638	20011120
	BG 107804	A	20040227	BG 2003-107804	20030512
	ZA 2003003887	A	20040621	ZA 2003-3887	20030519
	NO 2003002299	A	20030702	NO 2003-2299	20030521
PRAI	DE 2000-10057753	A1	20001122		
	DE 2001-10131987	A	20010702		
	WO 2001-EP12969	W	20011109		

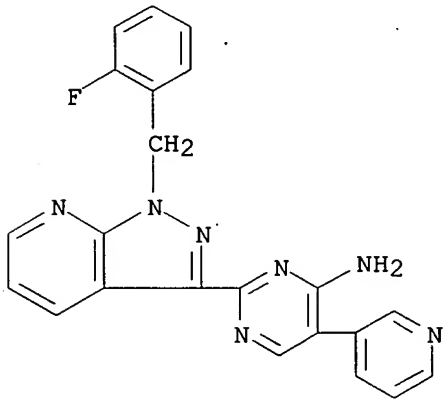
OS MARPAT 136:401774
AB Title compds. [I; R1 = 4-pyridinyl, 3-pyridinyl; R2 = H, halo, amino], were prepared Thus, a mixture of 1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxamidine (preparation given) and [(dimethylamino)methylene]pyridineacetonitrile (preparation given) in xylene was treated with BF3·OEt2 for 19 h at 140° to give 33% 2-(1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl)-5-(4-pyridinyl)-4-pyridinamine. The latter showed the vessel relaxation effect with IC50 = 0.66 μM.
IT **402595-29-3P 428828-78-8P 428828-82-4P**

428828-85-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinylpyrimidine-substituted pyrazolopyridines as inhibitors of cGMP degradation)

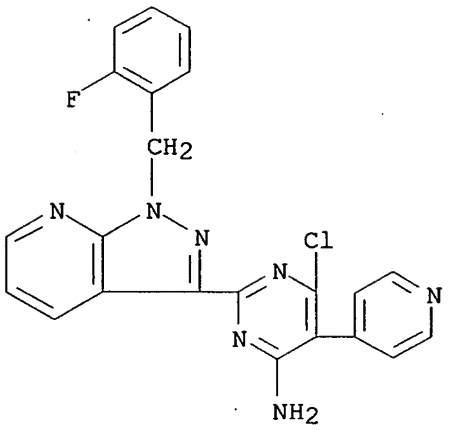
RN 402595-29-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



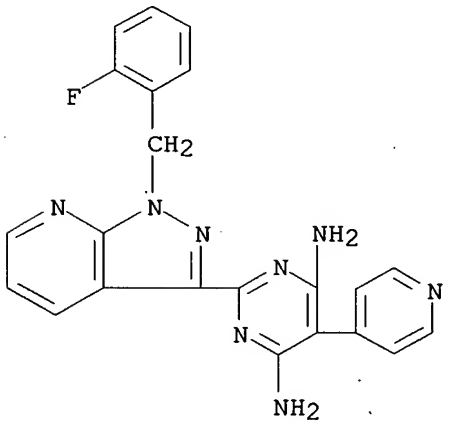
RN 428828-78-8 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(3-pyridinyl)- (9CI) (CA INDEX NAME)



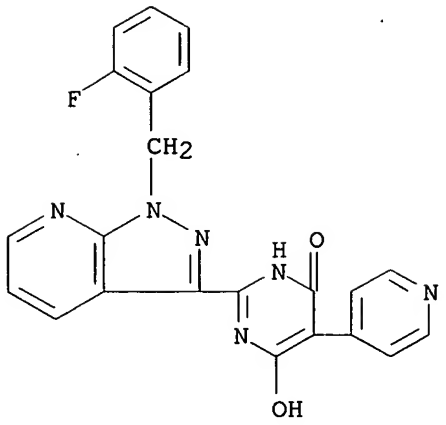
RN 428828-82-4 CAPLUS
CN 4-Pyrimidinamine, 6-chloro-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



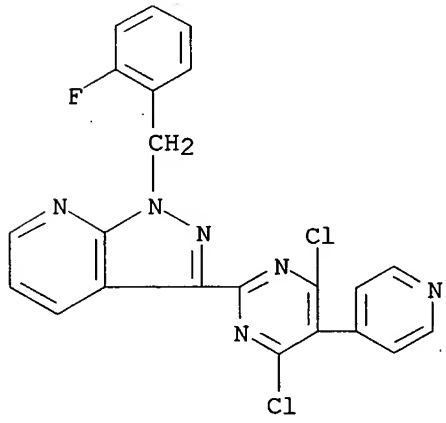
RN 428828-85-7 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



IT **428828-70-0P 428828-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridinylpyrimidine-substituted pyrazolopyridines as inhibitors of cGMP degradation)
RN 428828-70-0 CAPLUS
CN 4(1H)-Pyrimidinone, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-6-hydroxy-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 428828-74-4 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[4,6-dichloro-5-(4-pyridinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 45 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:391315 CAPLUS
DN 136:386130
TI Preparation of pyrimidinyllactam-substituted pyrazolopyridines as inhibitors of cGMP degradation
IN Stasch, Johannes-Peter; Feurer, Achim; Weigand, Stefan; Stahl, Elke; Flubacher, Dietmar; Alonso-Alija, Cristina; Wunder, Frank; Lang, Dieter; Dembowsky, Klaus; Straub, Alexander; Perzborn, Elisabeth
PA Bayer AG, Germany
SO Ger. Offen., 38 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10122895	A1	20020523	DE 2001-10122895	20010511
	CA 2429308	AA	20020530	CA 2001-2429308	20011109
	WO 2002042299	A1	20020530	WO 2001-EP12965	20011109
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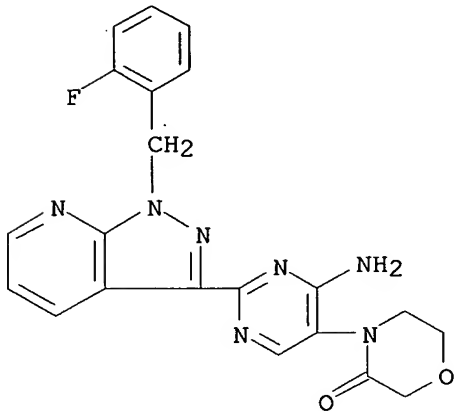
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002021827	A5	20020603	AU 2002-21827	20011109
	EP 1339716	A1	20030903	EP 2001-997487	20011109
	EP 1339716	B1	20041103		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004520285	T2	20040708	JP 2002-544433	20011109
	ES 2231581	T3	20050516	ES 2001-1997487	20011109
	US 6903089 X No DP.	B1	20050607	US 2003-432740	20011109
PRAI	DE 2000-10057752	A1	20001122		
	DE 2001-10122895	A	20010511		
	WO 2001-EP12965	W	20011109		

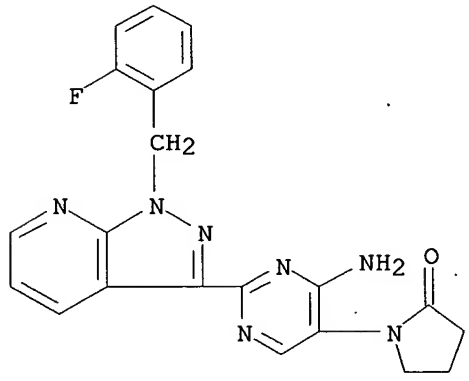
OS MARPAT 136:386130
AB Title compds. [I; R1 = NH2, NHCO(C1-6 alkyl); R2 = R3NCOR4; R3NCOR4 = (substituted) (annelated) 5-7 membered heterocyclyl containing an addnl. heteroatom] were prepared Thus, an E/Z mixture of 3-(dimethylamino)-2-(3-oxo-4-morpholinyl)-2-propanenitrile (preparation given) was stirred with 1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxamidine (preparation given) in xylene at 120° overnight to give 5.56% 4-(4-amino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl)-3-morpholinone. Several I showed a vessel relaxation effect with IC50 = 0.25-1.99 μM.
IT **426818-36-2P 426818-37-3P 426818-38-4P**
426818-39-5P 426818-40-8P 426818-41-9P
426818-42-0P 426818-43-1P 426818-44-2P
426818-45-3P 426818-46-4P 426818-47-5P
426818-48-6P 426818-49-7P 426818-50-0P
426818-51-1P 426818-52-2P 426818-53-3P
426818-54-4P 426818-55-5P 426818-56-6P
426818-57-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidinyllactam-substituted pyrazolopyridines as inhibitors of cGMP degradation)

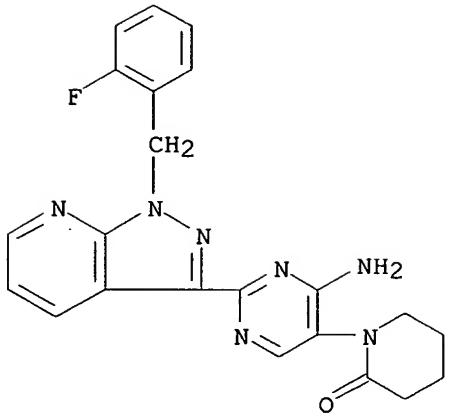
RN 426818-36-2 CAPLUS
CN 3-Morpholinone, 4-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



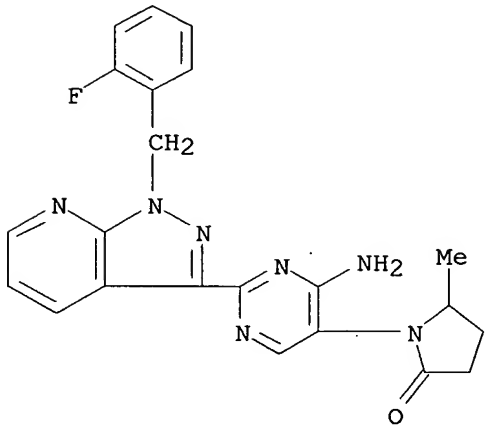
RN 426818-37-3 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



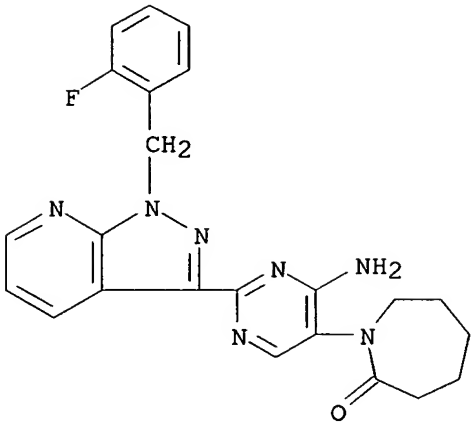
RN 426818-38-4 CAPLUS
CN 2-Piperidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



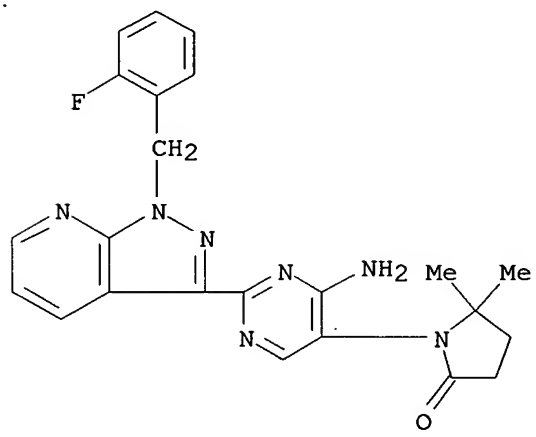
RN 426818-39-5 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5-methyl- (9CI) (CA INDEX NAME)



RN 426818-40-8 CAPLUS
CN 2H-Azepin-2-one, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]hexahydro- (9CI) (CA INDEX NAME)

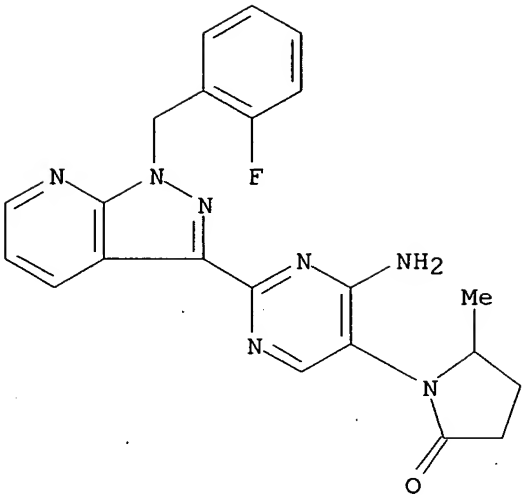


RN 426818-41-9 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



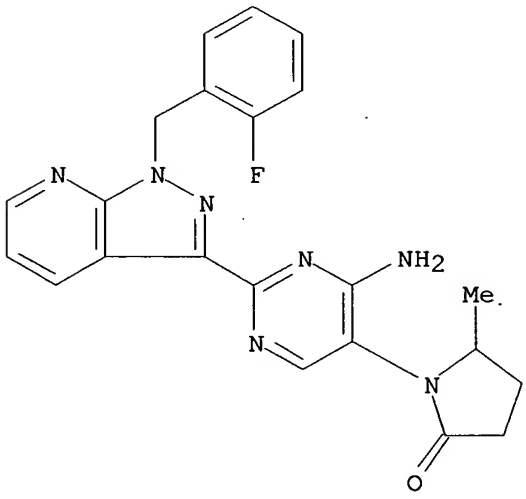
RN 426818-42-0 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5-methyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

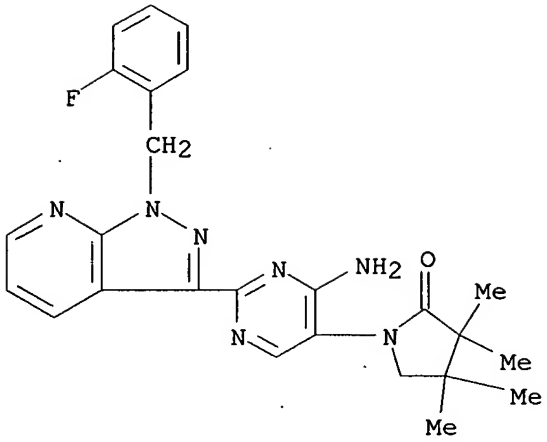


RN 426818-43-1 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5-methyl-, (-)- (9CI) (CA INDEX NAME)

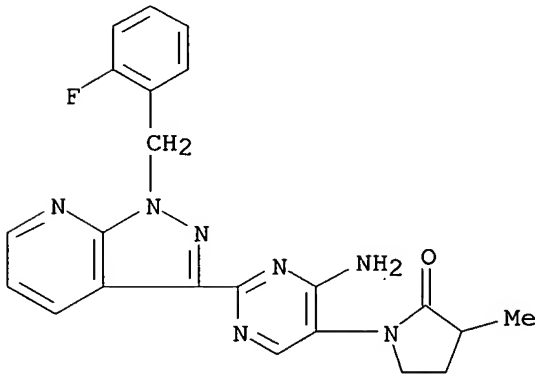
Rotation (-).



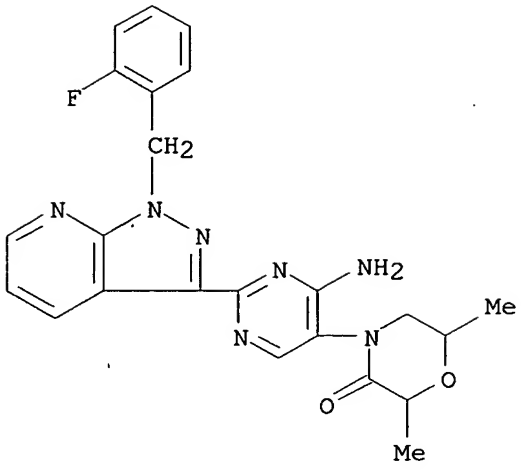
RN 426818-44-2 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-3,3,4,4-tetramethyl- (9CI) (CA INDEX NAME).



RN 426818-45-3 CAPLUS
CN 2-Pyrrolidinone, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-3-methyl- (9CI) (CA INDEX NAME)

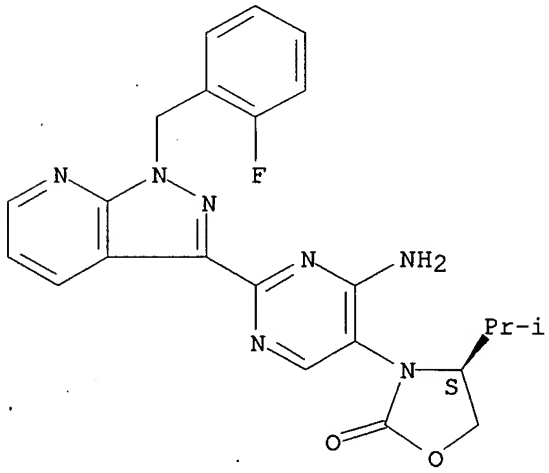


RN 426818-46-4 CAPLUS
CN 3-Morpholinone, 4-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-2,6-dimethyl- (9CI) (CA INDEX NAME)

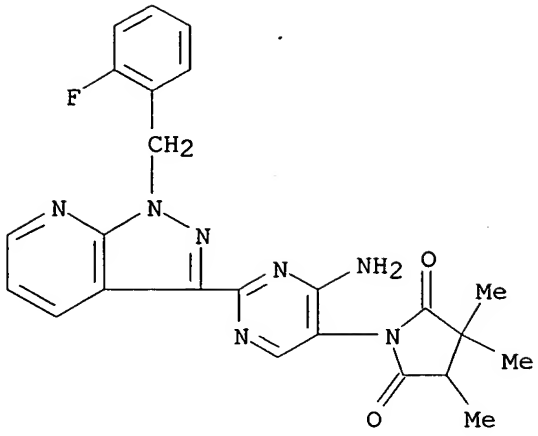


RN 426818-47-5 CAPLUS
CN 2-Oxazolidinone, 3-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-4-(1-methylethyl)-, (4S)- (9CI) (CA INDEX NAME)

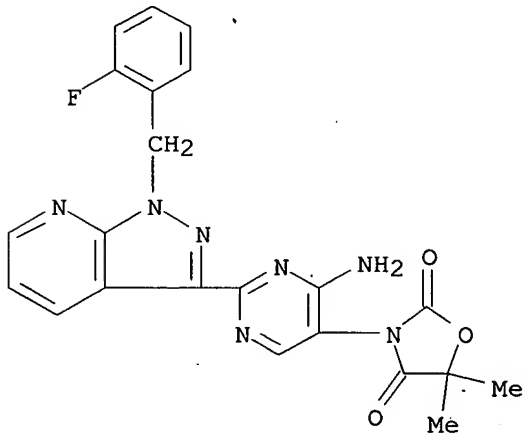
Absolute stereochemistry.



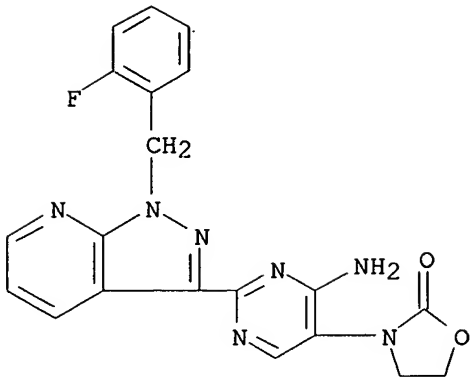
RN 426818-48-6 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-3,3,4-trimethyl- (9CI) (CA INDEX NAME)



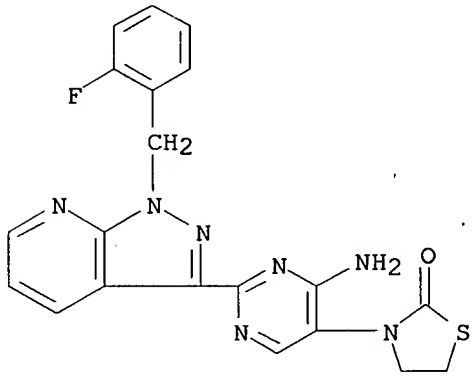
RN 426818-49-7 CAPLUS
CN 2,4-Oxazolidinedione, 3-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



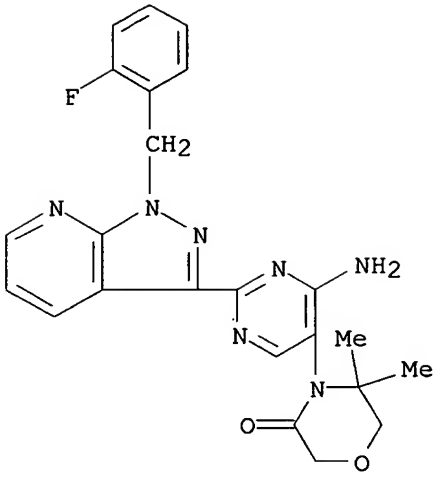
RN 426818-50-0 CAPLUS
CN 2-Oxazolidinone, 3-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



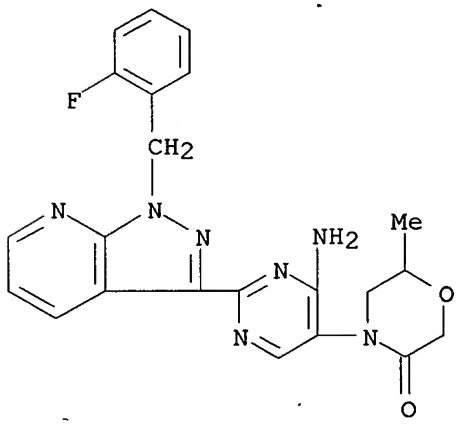
RN 426818-51-1 CAPLUS
CN 2-Thiazolidinone, 3-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



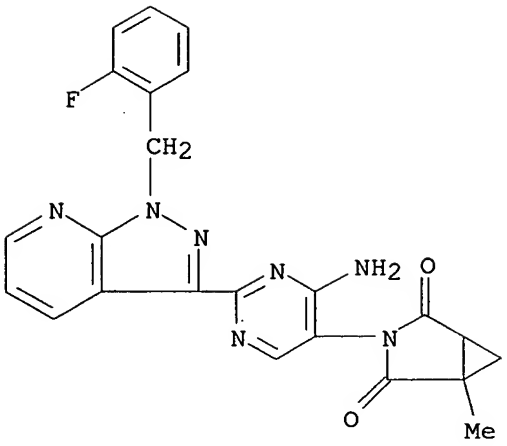
RN 426818-52-2 CAPLUS
CN 3-Morpholinone, 4-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



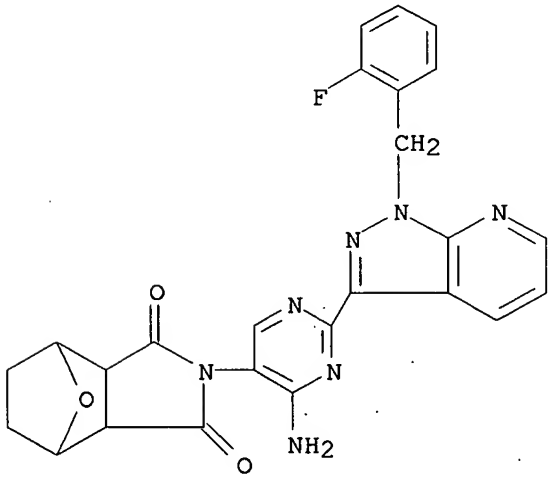
RN 426818-53-3 CAPLUS
CN 3-Morpholinone, 4-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-6-methyl- (9CI) (CA INDEX NAME)



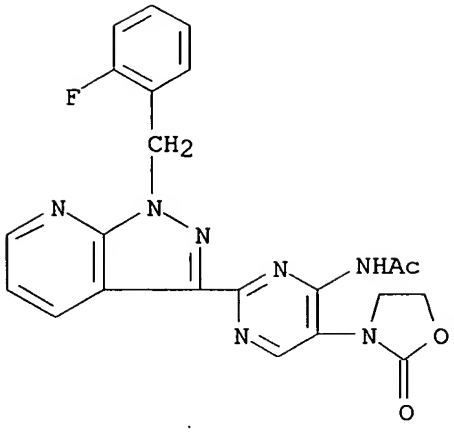
RN 426818-54-4 CAPLUS
CN 3-Azabicyclo[3.1.0]hexane-2,4-dione, 3-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]-1-methyl- (9CI) (CA INDEX NAME)



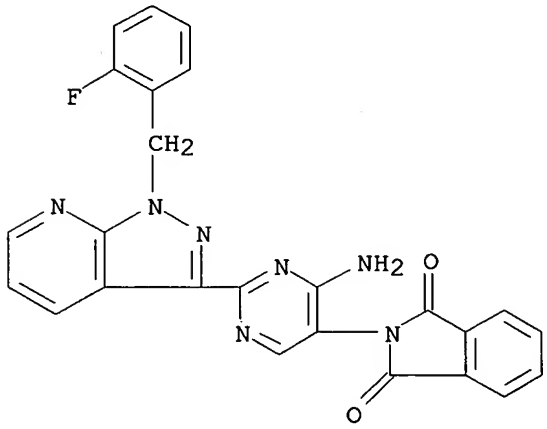
RN 426818-55-5 CAPLUS
CN 4,7-Epoxy-1H-isoindole-1,3(2H)-dione, 2-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]hexahydro- (9CI) (CA INDEX NAME)



RN 426818-56-6 CAPLUS
CN Acetamide, N-[2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(2-oxo-3-oxazolidinyl)-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



RN 426818-57-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 46 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:391284 CAPLUS
DN 136:401773
TI Preparation of pyrimidinylsulfonamide-substituted pyrazolopyridines as inhibitors of cGMP degradation
IN Stasch, Johannes-Peter; Feurer, Achim; Weigand, Stefan; Stahl, Elke; Flubacher, Dietmar; Alonso-Alija, Cristina; Wunder, Frank; Lang, Dieter; Dembowsky, Klaus; Straub, Alexander; Perzborn, Elisabeth
PA Bayer AG, Germany
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10057754	A1	20020523	DE 2000-10057754	20001122
	CA 2429313	AA	20020530	CA 2001-2429313	20011112
	WO 2002042302	A1	20020530	WO 2001-EP13064	20011112
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002027919	A5	20020603	AU 2002-27919	20011112
	EP 1339714	A1	20030903	EP 2001-989460	20011112
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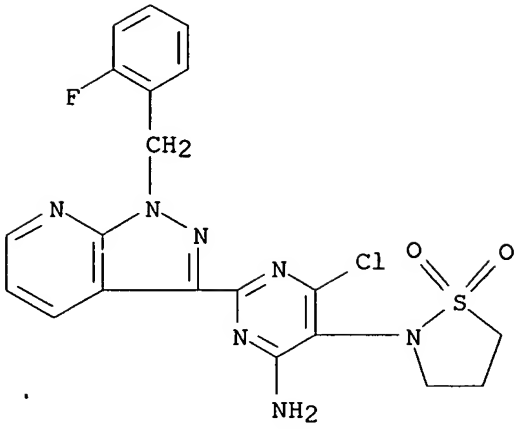
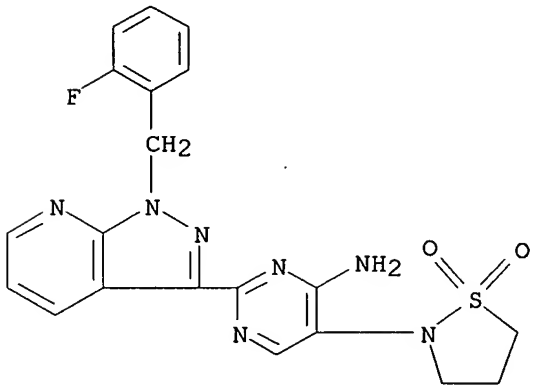
	JP 2004517828	T2	20040617	JP 2002-544436	20011112
	US 2004067937	A1	20040408	US 2003-432572	20031023
PRAI	DE 2000-10057754	A	20001122		
	WO 2001-EP13064	W	20011112		

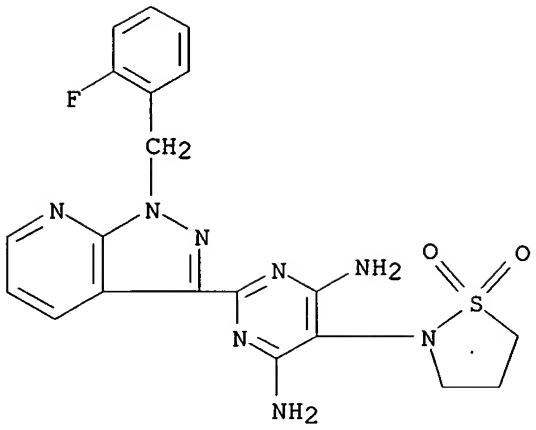
OS MARPAT 136:401773
AB Title compds. [I; R1 = H, Cl, amino; R2R3 together with the connected heteroatoms = (substituted) (N-, O-, S-interrupted) 5-7 membered heterocyclyl], were prepared Thus, 6-amino-5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinol (preparation given) was stirred with POCl2Ph for 2 h at 160° to give 60% 6-chloro-5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinamine. The latter showed the vessel relaxation effect with IC50 = 290 nM.
IT **428854-28-8P 428854-32-4P 428854-36-8P 428854-40-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidinylsulfonamide-substituted pyrazolopyridines as inhibitors of cGMP degradation)
RN 428854-28-8 CAPLUS
CN 4-Pyrimidinamine, 6-chloro-5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 428854-32-4 CAPLUS
CN 4-Pyrimidinamine, 5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

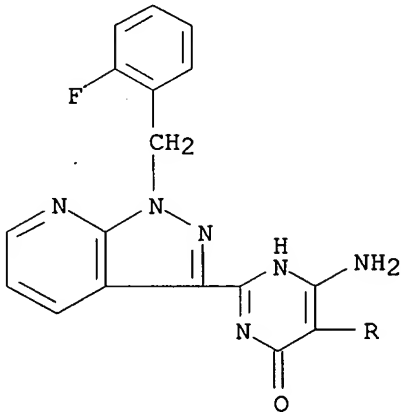


RN 428854-36-8 CAPLUS
CN 4,6-Pyrimidinediamine, 5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

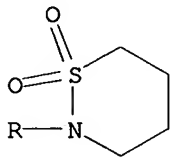


RN 428854-40-4 CAPLUS
CN 4(1H)-Pyrimidinone, 6-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)- (9CI) (CA INDEX NAME)

PAGE 1-A

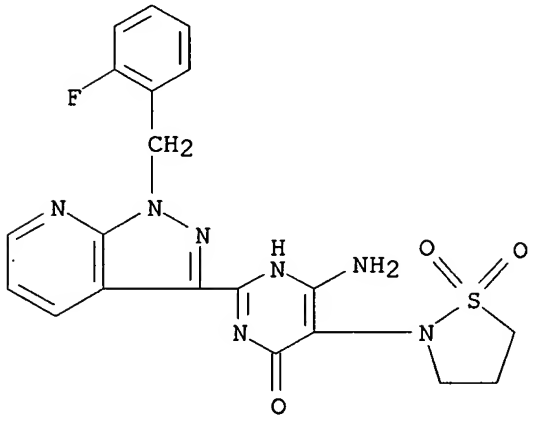


PAGE 2-A



IT **428854-26-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidinylsulfonamide-substituted pyrazolopyridines as inhibitors of cGMP degradation)
RN 428854-26-6 CAPLUS

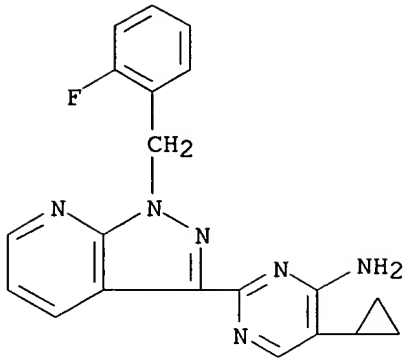
CN 4(1H)-Pyrimidinone, 6-amino-5-(1,1-dioxido-2-isothiazolidinyl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



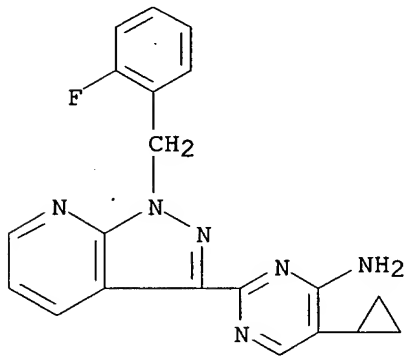
L4 ANSWER 47 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:347219 CAPLUS
DN 136:350594
TI Use of stimulators of soluble guanylate cyclase for the treatment of osteoporosis
IN Geiss, Volker; Sander, Erich; Stasch, Johannes-Peter; Straub, Alexander
PA Bayer A.-G., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10054278	A1	20020508	DE 2000-10054278	20001102
	WO 2002036120	A1	20020510	WO 2001-EP12159	20011022
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002023633	A5	20020515	AU 2002-23633	20011022
	CA 2427551	AA	20030510	CA 2001-2427551	20011022
	EP 1335723	A1	20030820	EP 2001-992572	20011022
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004512366	T2	20040422	JP 2002-538932	20011022
	US 2004053915	A1	20040318	US 2003-415708	20031022
PRAI	DE 2000-10054278	A	20001102		
	WO 2001-EP12159	W	20011022		

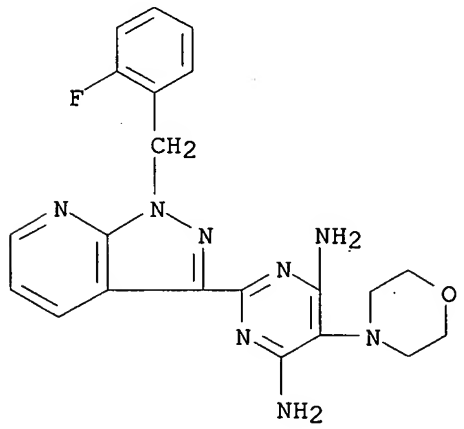
OS MARPAT 136:350594
AB The invention discloses the use of stimulators of soluble guanylate cyclase, in particular compds. I [R1 = (un)saturated (un)substituted C3-8 cycloalkyl, (un)saturated or partially unsatd. 3-8-membered heterocyclyl, which can contain 1-4 of N, O, S, SO, SO2 and be optionally substituted; R2 = H, NH2], as well as salts, isomers and hydrates thereof, for the production of a medicament for the treatment of osteoporosis.
IT **256376-24-6 256376-24-6D**, isomers, salts, and hydrates
256498-66-5 256498-66-5D, isomers, salts, and hydrates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soluble guanylate cyclase stimulators for treatment of osteoporosis)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



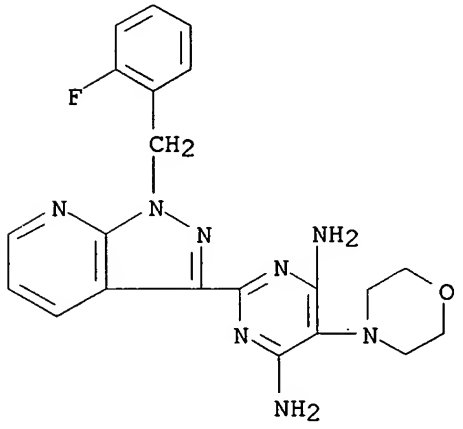
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



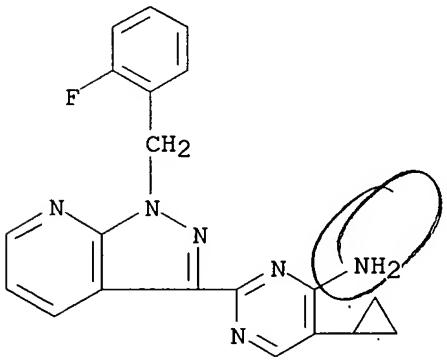
RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

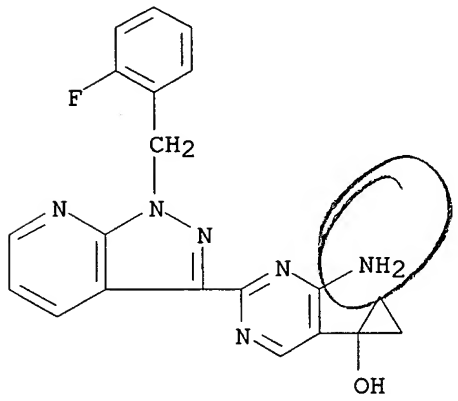


L4 ANSWER 48 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:268387 CAPLUS
DN 136:382099
TI BAY 41-2272 activates two isoforms of nitric oxide-sensitive guanylyl cyclase
AU Koglin, Markus; Stasch, Johannes-Peter; Behrends, Soenke
CS Institut fuer Experimentelle und Klinische Pharmakologie, Universitaet Hamburg, Hamburg, D-20246, Germany
SO Biochemical and Biophysical Research Communications (2002), 292(4), 1057-1062
CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
AB Soluble guanylyl cyclase (I) is an important target for endogenous NO and the guanylyl cyclase modulator, YC-1. Recently BAY 41-2272 was identified as a similar but more potent and more specific substance. Whereas YC-1 also acts as nonspecific phosphodiesterase inhibitor, BAY 41-2272 was devoid of an effect on phosphodiesterases. BAY 41-2272 has so far only been tested on the α1/β1 heterodimeric isoform of soluble I and its binding site has been mapped to a region in the α1 subunit N-terminal sequence. Although this region is poorly conserved in the α2 subunit, it is shown here that the α2/β1 heterodimeric enzyme isoform was activated by BAY 41-2272. Deletion anal. of the α2 subunit and co-expression with the β1 subunit in the baculovirus/Sf9 system was consistent with the N-terminal amino acids 104-401 of the α2 subunit as the binding site for BAY 41-2272.
IT **256376-24-6**, BAY 41-2272
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BAY 41-2272 activation of 2 isoforms of nitric oxide-sensitive guanylyl cyclase and its comparison with YC-1)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

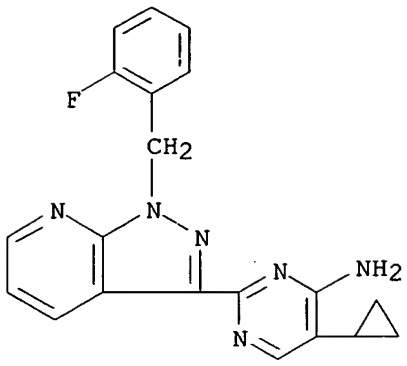


RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

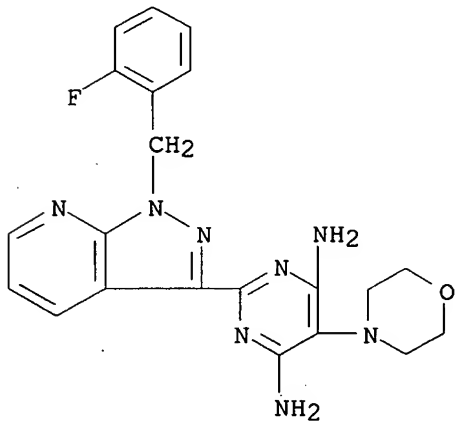
L4 ANSWER 49 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:251260 CAPLUS
DN 137:226160
TI Metabolites of Orally Active NO-Independent Pyrazolopyridine Stimulators of Soluble Guanylate Cyclase
AU Straub, Alexander; Benet-Buckholz, Jordi; Frode, Rita; Kern, Armin; Kohlsdorfer, Christian; Schmitt, Peter; Schwarz, Thomas; Siefert, Hans-Martin; Stasch, Johannes-Peter
CS Institute of Medicinal Chemistry, Bayer AG, Pharma Research Centre, Wuppertal, D-42096, Germany
SO Bioorganic & Medicinal Chemistry (2002), 10(6), 1711-1717
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB The pyrazolopyridine stimulators of soluble guanylate cyclase BAY 41-2272 and 41-8543 were oxidised in rats and dogs at their 5-pyrimidinyl-cyclopropyl and -morpholino residue. These metabolites activate the soluble guanylate cyclase, induce vasoelaxation and thereby may contribute to the in vivo activity of BAY 41-2272 and BAY 41-8543.
IT **304874-04-2P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolites of orally active NO-independent pyrazolopyridine stimulators of soluble guanylate cyclase)
RN 304874-04-2 CAPLUS
CN Cyclopropanol, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)



IT **256376-24-6**, BAY 41-2272 **256498-66-5**, BAY 41-8543
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of orally active NO-independent pyrazolopyridine stimulators of soluble guanylate cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

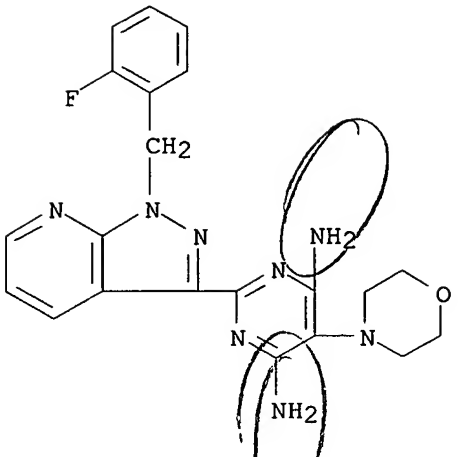


RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



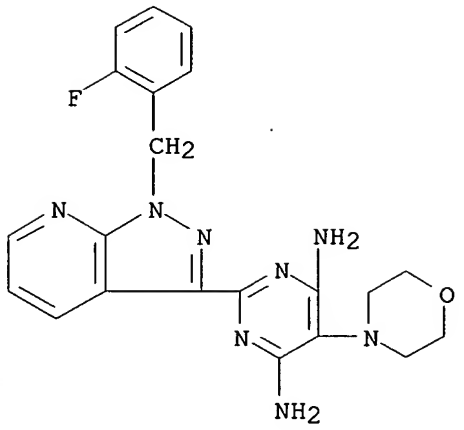
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 50 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:126828 CAPLUS
DN 137:447
TI Cardiovascular actions of a novel NO-independent guanylyl cyclase stimulator, BAY 41-8543: in vivo studies
AU Stasch, Johannes-Peter; Dembowsky, Klaus; Perzborn, Elisabeth; Stahl, Elke; Schramm, Matthias
CS Institute of Cardiovascular Research, Pharma Research Center, Bayer AG, Wuppertal, D-42096, Germany
SO British Journal of Pharmacology (2002), 135(2), 344-355
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB BAY 41-8543 is a novel non-NO-based stimulator of sGC. This study investigates the acute effects of BAY 41-8543 on hemodynamics in anesthetized rats and dogs, its long-term effects in conscious hypertension rat models and its antiplatelet effects. In anesthetized dogs, i.v. injections of BAY 41-8543 (3-100 μg kg-1) caused a dose-dependent decrease in blood pressure and cardiac oxygen consumption as well as an increase in coronary blood flow and heart rate. In anesthetized normotensive rats, BAY 41-8543 produced a dose-dependent and long-lasting blood pressure lowering effect after i.v. (3-300 μg kg-1) and oral (0.1-1 mg kg-1) administration. A dose-dependent and long-lasting decrease in blood pressure was also observed in conscious spontaneously hypertensive rats with a threshold dose of 0.1 mg kg-1 p.o. After 3 mg kg-1 the antihypertensive effect lasted for nearly 24 h. After multiple dosages, BAY 41-8543 did not develop tachyphylaxis in SHR. BAY 41-8543 prolonged the rat tail bleeding time and reduced thrombosis in the FeCl3 thrombosis model after oral administration. In a low NO, high renin rat model of hypertension, BAY 41-8543 prevented the increase in blood pressure evoked by L-NAME and reveals a kidney protective effect. In this model, the overall beneficial effects of BAY 41-8543 manifested as both antiplatelet effect and vasodilatation were reflected in a significant reduction in mortality. The pharmacol. profile of BAY 41-8543 suggests therefore that this compound has the potential to be an important research tool for in vivo investigations in the sGC/cGMP field and it also has the potential of being a unique clin. utility for treatment of cardiovascular diseases.
IT **256498-66-5**, BAY 41-8543
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cardiovascular actions of BAY 41-8543 (NO-independent guanylyl cyclase stimulator))
RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



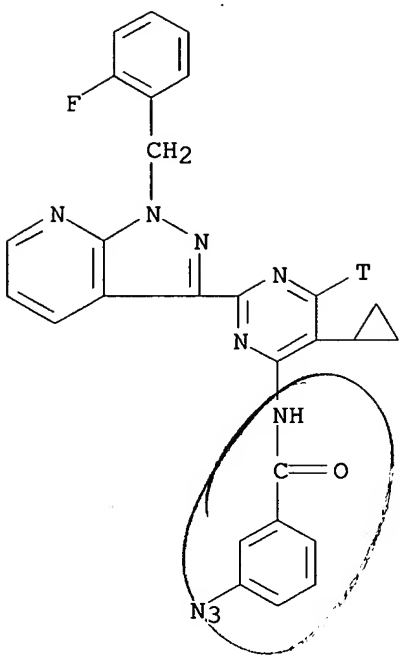
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 51 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:126827 CAPLUS
DN 137:446
TI Pharmacological actions of a novel NO-independent guanylyl cyclase stimulator, BAY 41-8543: in vitro studies
AU Stasch, Johannes-Peter; Alonso-Alija, Cristina; Apeler, Heiner; Dembowsky, Klaus; Feurer, Achim; Minuth, Torsten; Perzborn, Elisabeth; Schramm, Matthias; Straub, Alexander
CS Institute of Cardiovascular Research, Pharma Research Center, Bayer AG, Wuppertal, Q-42096, Germany
SO British Journal of Pharmacology (2002), 135(2), 333-343
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB BAY 41-8543 is a novel, highly specific and so far the most potent NO-independent stimulator of sGC. Here we report the effects of BAY 41-8543 on the isolated enzyme, endothelial cells, platelets, isolated vessels and Langendorff heart preparation BAY 41-8543 stimulates the recombinant sGC concentration-dependently from 0.0001 μM to 100 μM up to 92-fold. In combination, BAY 41-8543 and NO have synergistic effects over a wide range of concns. Similar results are shown in implying that BAY 41-8543 stimulates the sGC directly and furthermore makes the enzyme more sensitive to its endogenous activator NO. In vitro, BAY 41-8543 is a potent relaxing agent of aortas, saphenous arteries, coronary arteries and veins with IC50-values in the nM range. In the rat heart Langendorff preparation, BAY 41-8543 potently reduces coronary perfusion pressure from 10-9 to 10-6 g ml-1 without any effect on left ventricular pressure and heart rate. BAY 41-8543 is effective even under nitrate tolerance conditions proved by the same vasorelaxing effect on aortic rings taken either from normal or nitrate-tolerant rats. BAY 41-8543 is a potent inhibitor of collagen-mediated aggregation in washed human platelets (IC50=0.09 μM). In plasma, BAY 41-8543 inhibits collagen-mediated aggregation better than ADP-induced aggregation, but has no effect on the thrombin pathway. BAY 41-8543 is also a potent direct stimulator of the cGMP/PKG/VASP pathway in platelets and synergizes with NO over a wide range of concns. These results suggest that BAY 41-8543 is on the one hand an invaluable tool for studying sGC signaling in vitro and on the other hand its unique profile may offer a novel approach for treating cardiovascular diseases.
IT **256498-66-5**, BAY 41-8543
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro pharmacol. actions of a novel NO-independent guanylyl cyclase stimulator, BAY 41-8543)
RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

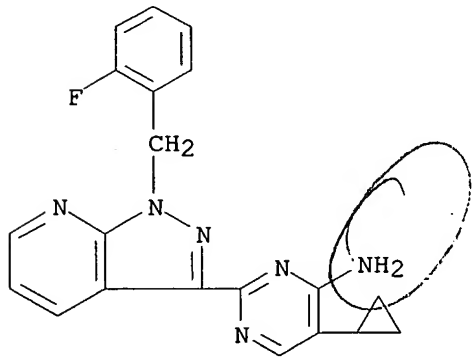


RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

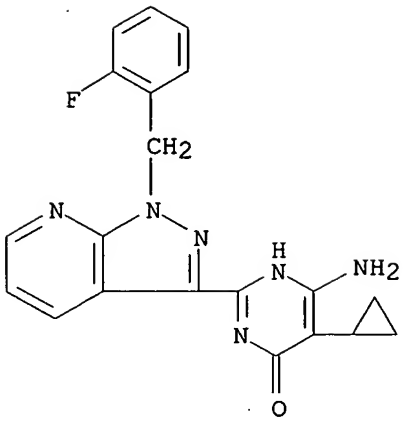
L4 ANSWER 52 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:126818 CAPLUS
DN 137:228525
TI NO-independent regulatory site of direct sGC stimulators like YC-1 and BAY 41-2272
AU Becker, Eva Maria; Alonso-Alija, Cristina; Apeler, Heiner; Gerzer, Rupert; Minuth, Torsten; Pleiss, Ulrich; Schmidt, Peter; Schramm, Matthias; Schroeder, Henning; Schroeder, Werner; Steinke, Wolfram; Straub, Alexander; Stasch, Johannes-Peter
CS Pharma Res. Center, Bayer AG, Wuppertal, Germany
SO BMC Pharmacology [online computer file] (2001), 1, No pp. given
CODEN: BPMHBU; ISSN: 1471-2210
URL: http://www.biomedcentral.com/1471-2210/1/13
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
OS CASREACT 137:228525
AB Background: The most important receptor for nitric oxide is the soluble guanylate cyclase (sGC), a heme containing heterodimer. Recently, a pyrazolopyridine derivative BAY 41-2272, structurally related to YC-1, was identified stimulating soluble guanylate cyclase in an NO-independent manner, which results in vasodilation and antiplatelet activity. The study described here addresses the identification of the NO-independent site on soluble guanylate cyclase. Results: We developed a photoaffinity label (3H-meta-PAL) for the direct and NO-independent soluble guanylate cyclase (sGC) stimulator BAY 41-2272 by introducing an azido-group into the tritium labeled compound The synthesized photoaffinity label directly stimulates the purified sGC and shows in combination with NO a synergistic effect on SGC activity. Irradiation with UV light of 3H-meta-PAL together with the highly purified sGC leads to covalent binding to the α1-subunit of the enzyme. This binding is blocked by unlabeled meta-PAL, YC-1 and BAY 41-2272. For further identification of the NO-independent regulatory site the 3H-meta-PAL labeled sGC was fragmented by CNBr digest. The 3H-meta-PAL binds to a CNBr fragment, consisting of the amino acids 236-290 of the α1-subunit. Determination of radioactivity of the single PTH-cycles from the sequencing of this CNBr fragment detected the cysteine 238 as binding residues of the 3H-meta-PAL. Conclusions: Our data demonstrate that the region surrounding the cysteine 238 and 243 in the α1-subunit of the sGC could play an important role in regulation of sGC activity and could be the target of this new type of sGC stimulators.
IT **457923-59-0P**
RL: ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(NO-independent regulatory site of direct sGC stimulators like YC-1 and BAY 41-2272)
RN 457923-59-0 CAPLUS
CN Benzamide, 3-azido-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-1,6-dihydro-4-pyrimidinyl-6-t]- (9CI) (CA INDEX NAME)



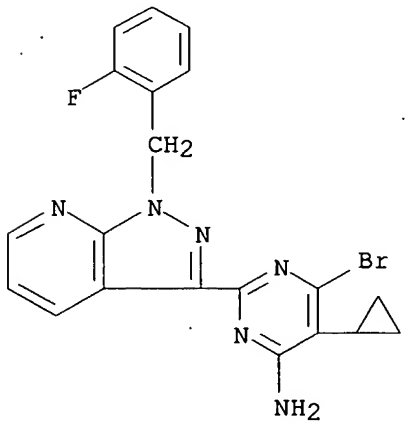
IT **256376-24-6,** BAY 412272
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(NO-independent regulatory site of direct sGC stimulators like YC-1 and BAY 41-2272)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



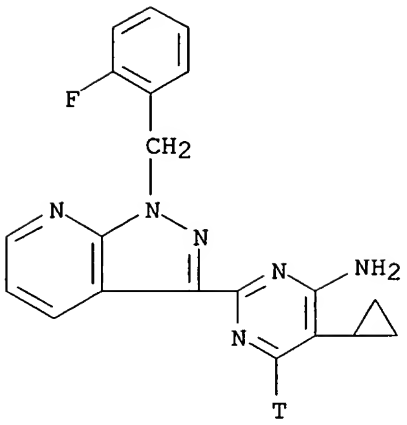
IT **457923-53-4P 457923-55-6P 457923-57-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(NO-independent regulatory site of direct sGC stimulators like YC-1 and BAY 41-2272)
RN 457923-53-4 CAPLUS
CN 4(1H)-Pyrimidinone, 6-amino-5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 457923-55-6 CAPLUS
CN 4-Pyrimidinamine, 6-bromo-5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)

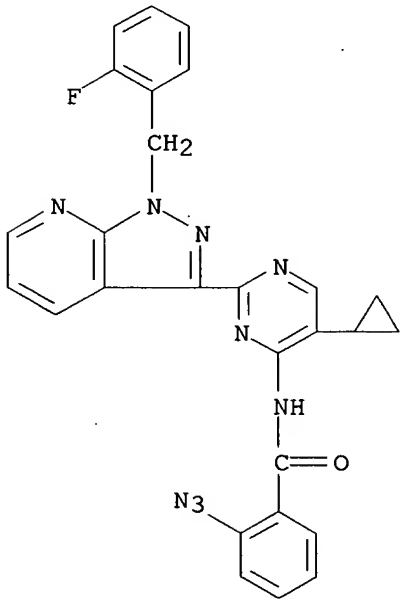


RN 457923-57-8 CAPLUS
CN 4-Pyrimidin-6-t-amine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-1,6-dihydro- (9CI) (CA INDEX NAME)

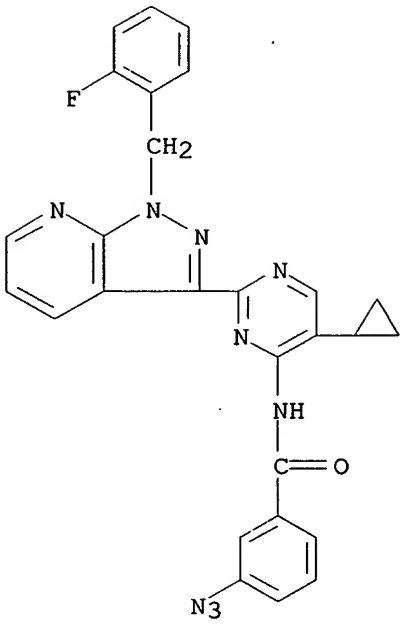


IT **459126-11-5P**, BAY 50-6038 **459126-13-7P**, BAY 51-9491
459126-15-9P, BAY 50-8364
RL: SPN (Synthetic preparation); PREP (Preparation)
(NO-independent regulatory site of direct sGC stimulators like YC-1 and BAY 41-2272)

RN 459126-11-5 CAPLUS
CN Benzamide, 2-azido-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

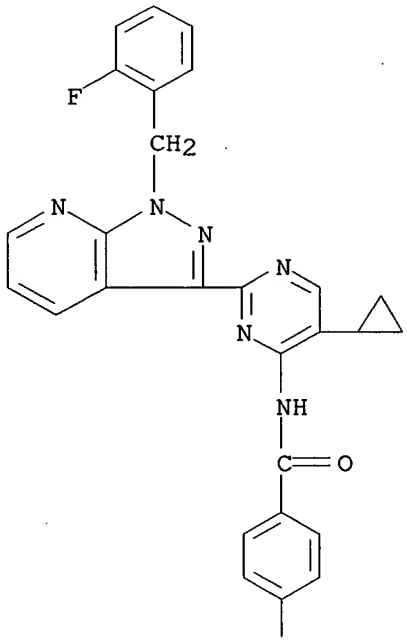


RN 459126-13-7 CAPLUS
CN Benzamide, 3-azido-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



RN 459126-15-9 CAPLUS
CN Benzamide, 4-azido-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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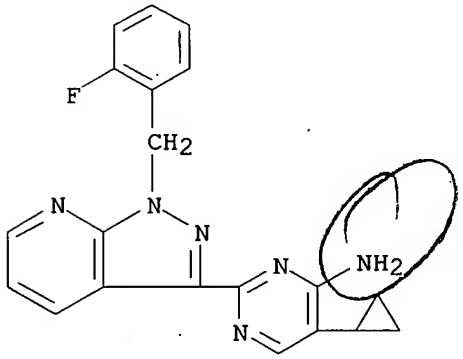
N_3

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 53 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:810514 CAPLUS
DN 136:144457
TI cGMP signalling beyond nitric oxide
AU Mayer, Bernd; Koesling, Doris
CS Institut fur Pharmakologie und Toxikologie, Karl-Franzens-Universitat Graz, Graz, A-8010, Austria
SO Trends in Pharmacological Sciences (2001), 22(11), 546-548
CODEN: TPHSDY; ISSN: 0165-6147
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review. Many of the physiol. effects of nitric oxide are mediated by activation of soluble guanylyl cyclase, resulting in cellular cGMP accumulation. In the 1990s, the benzylindazole derivative YC-1 was identified as a novel modulator of cGMP signaling that exerted complex actions in a NO-independent manner. A recent study describes a high-affinity YC-1 analog that decreases blood pressure in hypertensive rats and increases bleeding time, which suggests that this drug might have therapeutic potential as a vasodilator with antiplatelet activity.
IT **256376-24-6**, BAY 412272
RL: PAC (Pharmacological activity); BIOL (Biological study)
(cGMP signalling beyond nitric oxide)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 54 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:479149 CAPLUS
DN 135:81981
TI Method for micronization of cardiovascular agents by co-grinding the active substance and lactose
IN Laich, Tobias
PA Bayer A.-G., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19962926	A1	20010628	DE 1999-19962926	19991224
WO 2001047494	A1	20010705	WO 2000-EP12569	20001212

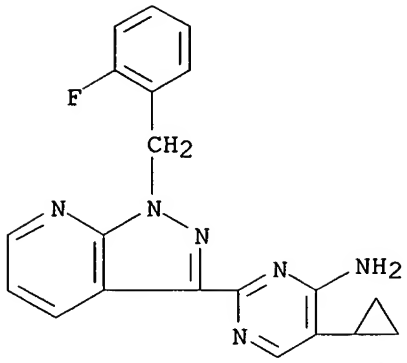
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DE 1999-19962926 A 19991224

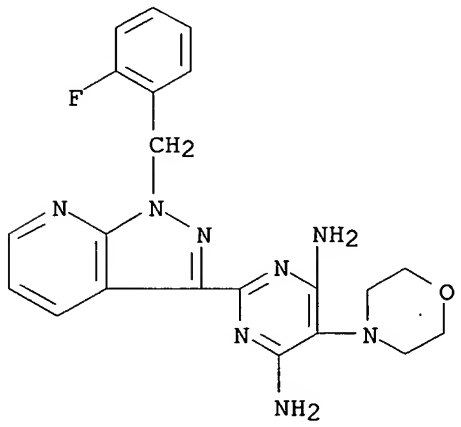
AB The invention concerns the preparation of micronized cardiovascular agents for oral drug delivery systems by co-grinding the active ingredient with lactose. Thus 136,84 g 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyridinamine and 54.73 g lactose (200 mesh) were mixed in a tubular mixer at 30 U/min for 10 min. The mixture was micronized in a steel spiral mill at injection pressure 5 bar, grinding pressure 4.5 bar for 25 min. To the micronized mixture 0.49 g sodium lauryl sulfate, 5.95 g sodium CM-cellulose and 1.98 g magnesium stearate were added, and mixed again in the tubular mixer at 30 U/min for 5 min. Finally 146.15 mg tablets were pressed.

IT **256376-24-6 256498-66-5**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for micronization of cardiovascular agents by co-grinding active substance and lactose)

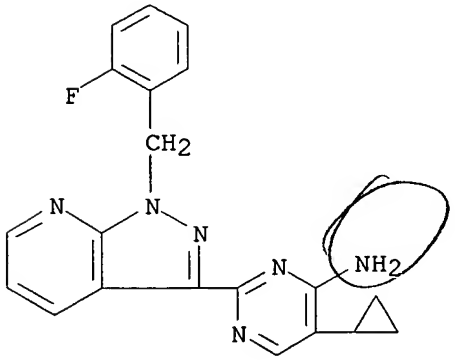
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



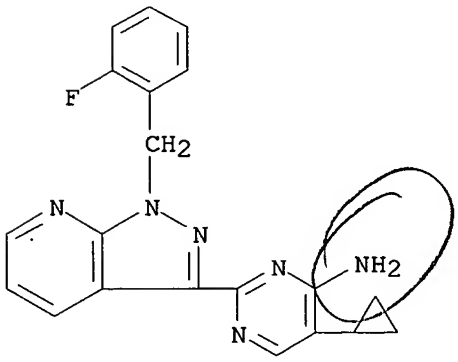
RN 256498-66-5 CAPLUS
CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)



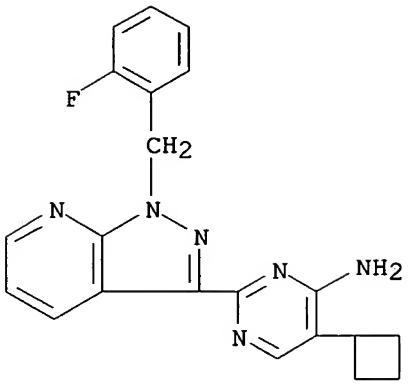
L4 ANSWER 55 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:208883 CAPLUS
DN 135:28855
TI NO-independent regulatory site on soluble guanylate cyclase
AU Stasch, Johannes-Peter; Becker, Eva Maria; Alonso-Alija, Cristina; Apeler, Heiner; Dembowsky, Klaus; Feurer, Achim; Gerzer, Rupert; Minuth, Torsten; Perzborn, Elisabeth; Pleiss, Ulrich; Schroder, Henning; Schroeder, Werner; Stahl, Eike; Steinke, Wolfram; Straub, Alexander; Schramm, Mathias
CS Pharma Res. Center, Bayer AG, Wuppertal, D-42096, Germany
SO Nature (London, United Kingdom) (2001), 410(6825), 212-215
CODEN: NATUAS; ISSN: 0028-0836
PB Nature Publishing Group
DT Journal
LA English
AB Nitric oxide (NO) is a widespread, potent, biol. mediator that has many physiol. and pathophysiol. roles. Research in the field of NO appears to have followed a straightforward path, and the findings have been progressive: NO and cGMP are involved in vasodilatation; glycerol trinitrate relaxes vascular smooth muscles by bioconversion to NO; mammalian cells synthesize NO; and last, NO mediates vasodilation by stimulating the soluble guanylate cyclase (sGC), a heterodimeric (α/β) heme protein that converts GTP to cGMP. Here the authors report the discovery of a regulatory site on sGC. Using photoaffinity labeling, the authors have identified the cysteine 238 and cysteine 243 region in the α1-subunit of sGC as the target for a new type of sGC stimulator. Moreover, the authors present a pyrazolopyridine, BAY 41-2272, that potently stimulates sGC through this site by a mechanism that is independent of NO. This results in antiplatelet activity, a strong decrease in blood pressure and an increase in survival in a low-NO rat model of hypertension, and as such may offer an approach for treating cardiovascular diseases.
IT **256376-24-6**, BAY 41-2272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide-independent regulatory site on soluble guanylate cyclase that is stimulated by pyrazolopyridine BAY 41-2272 in relation to antihypertensive and antiplatelet activity)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



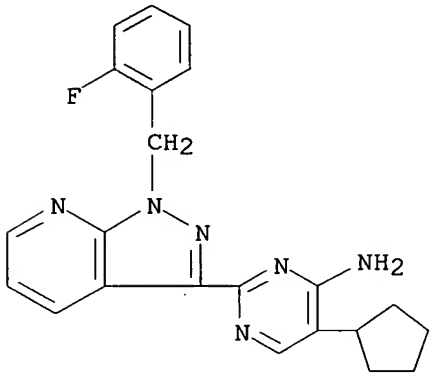
L4 ANSWER 56 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:207062 CAPLUS
DN 135:40411
TI NO-Independent stimulators of soluble guanylate cyclase
AU Straub, A.; Stasch, J.-P.; Alonso-Alija, C.; Benet-Buchholz, J.; Ducke, B.; Feurer, A.; Furstner, C.
CS Pharma Research Centre, Institute of Medicinal Chemistry, Bayer AG, Wuppertal, D-42096, Germany
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(6), 781-784
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB SARs around a novel type of guanylate cyclase stimulator which act by a mechanism different from classical NO-donors are described. Several pyrazolopyridinylpyrimidines are shown to relax aortic rings and revealed a long-lasting blood pressure lowering effect in rats after oral application. The SARs around a novel type of stimulators of soluble guanylate cyclase, their relaxing effects on preconstricted rabbit aortic rings (measured as IC50s) and their hypotensive properties are described.
IT **256376-24-6P**, Bay 41-2272
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NO-independent stimulators of soluble guanylate cyclase)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



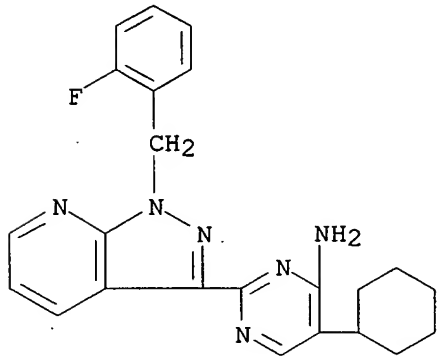
IT **256376-81-5 256376-82-6 256376-83-7 256376-85-9 344773-51-9 344773-55-3 344773-59-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NO-independent stimulators of soluble guanylate cyclase)
RN 256376-81-5 CAPLUS
CN 4-Pyrimidinamine, 5-cyclobutyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



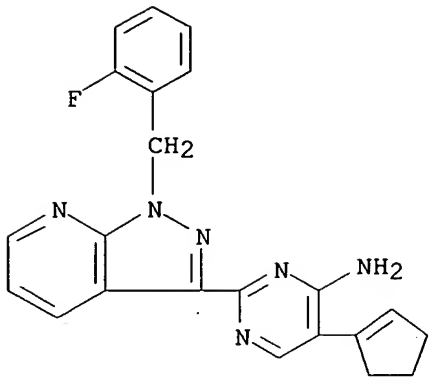
RN 256376-82-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopentyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



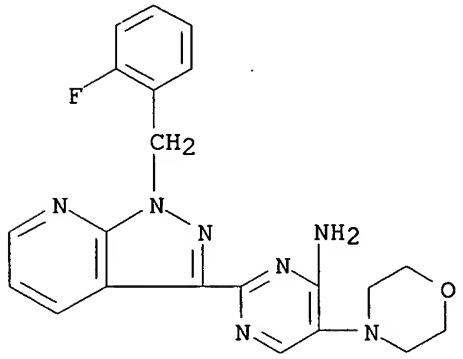
RN 256376-83-7 CAPLUS
CN 4-Pyrimidinamine, 5-cyclohexyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



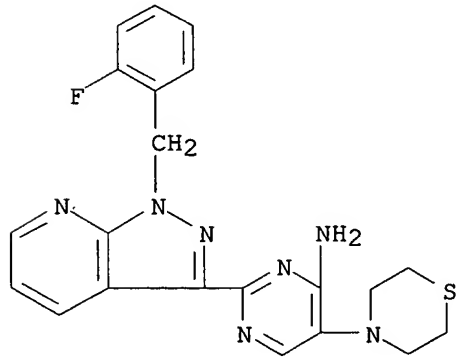
RN 256376-85-9 CAPLUS
CN 4-Pyrimidinamine, 5-(1-cyclopenten-1-yl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 344773-51-9 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

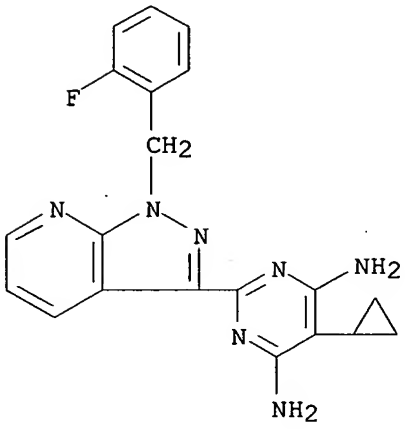


RN 344773-55-3 CAPLUS
CN 4-Pyrimidinamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-thiomorpholinyl)- (9CI) (CA INDEX NAME)



RN 344773-59-7 CAPLUS

CN 4,6-Pyrimidinediamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



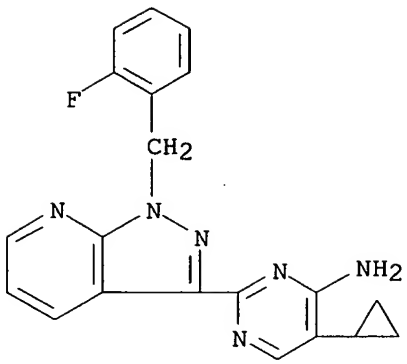
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:179663 CAPLUS
DN 134:222725
TI Preparation of 3-(4-amino-5-cycloalkylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridines from 1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxamidine hydrochloride and 2-cycloalkyl-2-cyanoethenyl esters.
IN Jaenichen, Jan; Preiss, Michael; Alonso-alija, Cristina; Straub, Alexander
PA Bayer AG, Germany
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19942809	A1	20010315	DE 1999-19942809	19990908
WO 2001017998	A2	20010315	WO 2000-EP8362	20000828
WO 2001017998	A3	20011011		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

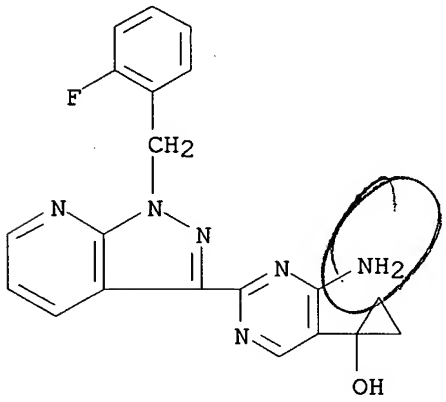
PRAI DE 1999-19942809 A 19990908
OS MARPAT 134:222725
AB Title compds. [I; R1 = (unsatd.) (substituted) cycloalkyl], were prepared by reaction of amidine (II) with R10CO2C:HCR1CN (R1 as above; R10 = alkyl) in an organic solvent in the presence of base. Thus, II (preparation given) and 2-cyano-2-cyclopropylethenyl acetate (preparation given) in THF were treated with KOCMe3 in THF at <40° followed by stirring for 2 h, cooling to 5-10°, and treatment with HOAc/Ac2O to give 84.3% I (R1 = cyclopropyl).
IT **256376-24-6P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of aminocycloalkylpyrimidinylfluorobenzylpyrazolopyridines from (fluorobenzyl)pyrazolopyridinecarboxamidine and cycloalkylcyanoethenyl esters)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)


F
CH2
N
N
N
N
NH2
N

L4 ANSWER 58 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:790500 CAPLUS
DN 133:350132
TI Preparation of cyclopropylpyrimidazinylpyridinopyrazole derivative for treatment of cardiovascular diseases.
IN Straub, Alexander; Feurer, Achim; Alonso-Alija, Cristina; Stahl, Elke; Stasch, Johannes-Peter; Perzborn, Elisabeth; Dembowsky, Klaus; Kern, Armin
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000066582	A1	20001109	WO 2000-EP3620	20000420
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19920352	A1	20001109	DE 1999-19920352	19990504
PRAI DE 1999-19920352	A	19990504		

AB The substituted pyrazole derivative (I) is claimed and well as its method of preparation and use in the treatment of cardiovascular diseases. Thus, I was prepared in a multistep process starting with Na salt of Et cyano-2-oxopropanoate and 2-fluorobenzylhydrazine.
IT **304874-04-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation for treatment of cardiovascular diseases)
RN 304874-04-2 CAPLUS
CN Cyclopropanol, 1-[4-amino-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-pyrimidinyl]- (9CI) (CA INDEX NAME)

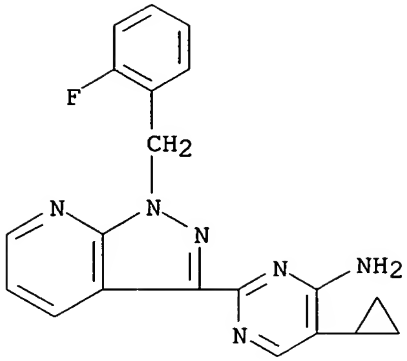


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

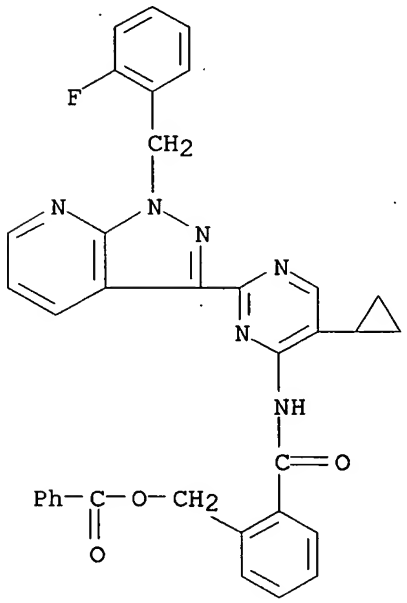
L4 ANSWER 59 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:83169 CAPLUS
DN 132:122629
TI Preparation of pyrimidinylpyrazolopyridines and related compounds as cardiovascular agents.
IN Straub, Alexander; Feurer, Achim; Alonso-Alija, Cristina; Stahl, Elke; Stasch, Johannes-Peter; Perzborn, Elisabeth; Huetter, Joachim; Dembowsky, Klaus
PA Bayer A.-G., Germany
SO Ger. Offen., 36 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19834047	A1	20000203	DE 1998-19834047	19980729
	WO 2000006568	A1	20000210	WO 1999-EP5073	19990716
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9952839	A1	20000221	AU 1999-52839	19990716
	EP 1102767	A1	20010530	EP 1999-938272	19990716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002521482	T2	20020716	JP 2000-562370	19990716
	US 6833364	B1	20041221	US 2001-744703	20010326
PRAI	DE 1998-19834047	A	19980729		
	WO 1999-EP5073	W	19990716		

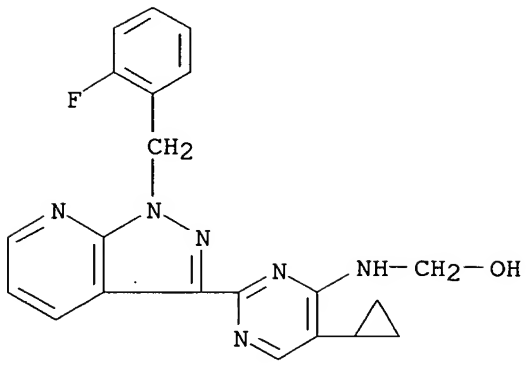
OS MARPAT 132:122629
AB Title compds. [I; ≥1 of R1, X, Y = (substituted) (unsatd.) cycloalkyl, the rest = H, amino, N3, CHO, SH, OH, CO2H, acyl, alkoxy, etc.; R2R3 = atoms to form (substituted) Ph, 6-membered saturated or aromatic heteroaryl; A = (substituted) 5-6 membered aromatic or saturated heterocyclic ring], were prepared Thus, 3-(4-amino-5-cyclopropylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine (preparation from 2-cyclopropyl-3-dimethylaminoacrylonitrile and the corresponding amidine given) inhibited thrombocyte aggregation with IC50 = 3 nM.
IT **256376-24-6P 256376-27-9P 256376-31-5P**
256376-34-8P 256376-39-3P 256376-43-9P
256376-49-5P 256376-54-2P 256376-81-5P
256376-82-6P 256376-83-7P 256376-85-9P
256376-86-0P 256376-87-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidinylpyrazolopyridines and related compds. as cardiovascular agents)
RN 256376-24-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



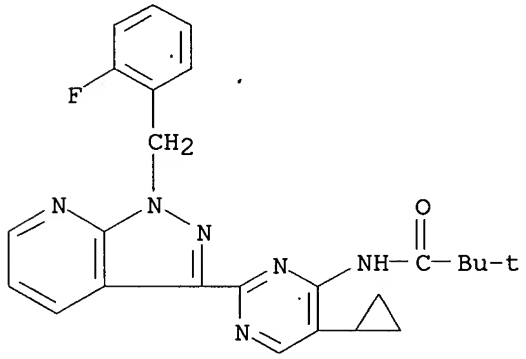
RN 256376-27-9 CAPLUS
CN Benzamide, 2-[(benzoyloxy)methyl]-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



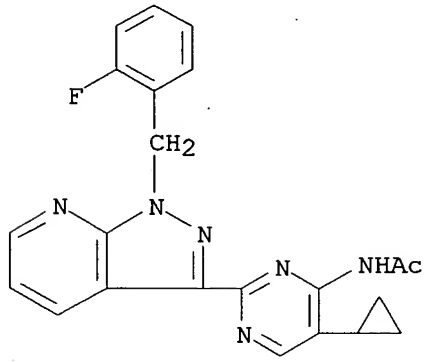
RN 256376-31-5 CAPLUS
CN Methanol, [[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]amino]- (9CI) (CA INDEX NAME)



RN 256376-34-8 CAPLUS
CN Propanamide, N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

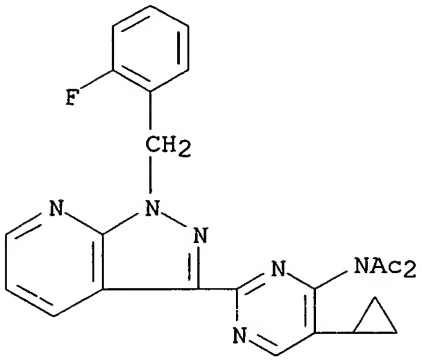


RN 256376-39-3 CAPLUS
CN Acetamide, N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

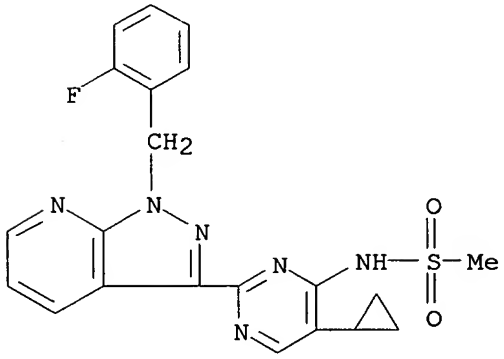


RN 256376-43-9 CAPLUS

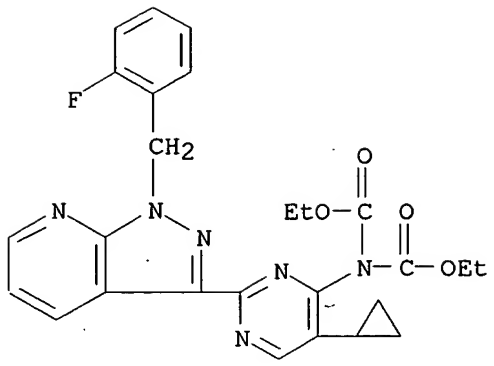
CN Acetamide, N-acetyl-N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



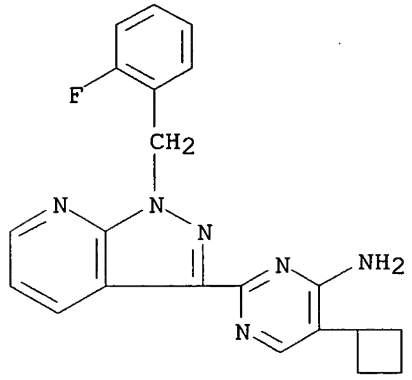
RN 256376-49-5 CAPLUS
CN Methanesulfonamide, N-[5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)



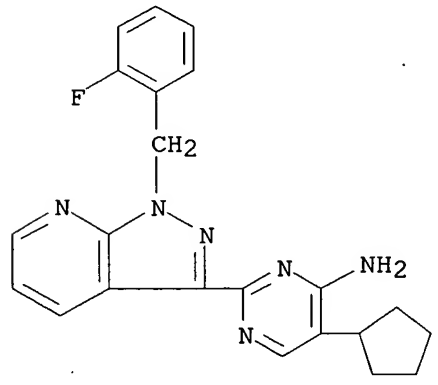
RN 256376-54-2 CAPLUS
CN Imidodicarbonic acid, [5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-pyrimidinyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 256376-81-5 CAPLUS
CN 4-Pyrimidinamine, 5-cyclobutyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256376-82-6 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopentyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256376-83-7 CAPLUS
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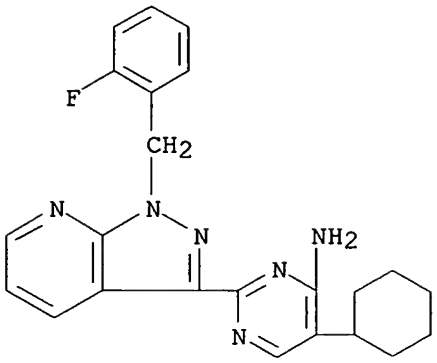
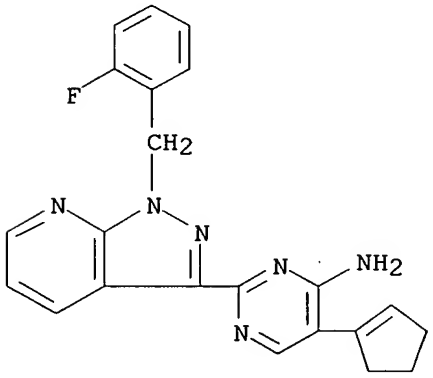
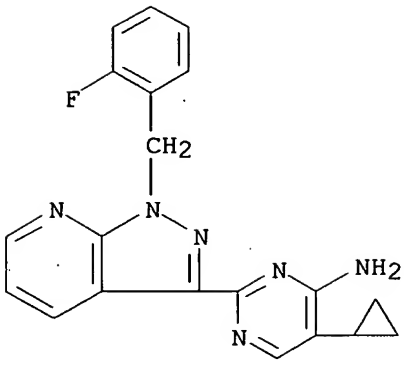
pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256376-85-9 CAPLUS
CN 4-Pyrimidinamine, 5-(1-cyclopenten-1-yl)-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 256376-86-0 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



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RN 256376-87-1 CAPLUS
CN 4-Pyrimidinamine, 5-cyclopropyl-2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

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CRN 256376-24-6
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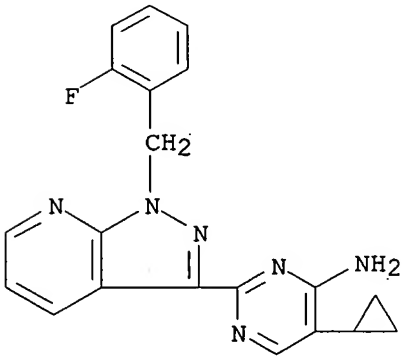

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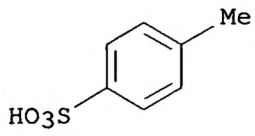
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L4 ANSWER 60 OF 60 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:83167 CAPLUS
DN 132:137382
TI Preparation of benzylpyrazolopyridines and related compounds as cardiovascular agents.
IN Straub, Alexander; Feurer, Achim; Alonso-Alija, Cristina; Stasch, Johannes-Peter; Perzborn, Elisabeth; Huetter, Joachim; Dembowsky, Klaus; Stahl, Elke
PA Bayer A.-G., Germany
SO Ger. Offen., 36 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19834044	A1	20000203	DE 1998-19834044	19980729
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	WO 1999-EP5074	W	19990716		
	US 2001-744830	A3	20010411		

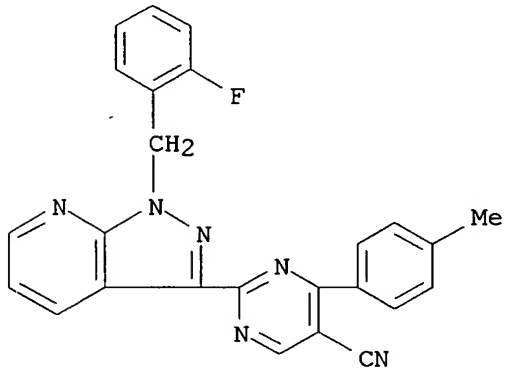
OS MARPAT 132:137382
AB Title compds.[I; R1 = saturated or aromatic 5-6 membered (substituted) heterocyclyl, etc.; R2R3 = atoms to form a 6-membered saturated or aromatic (substituted) heterocyclyl; A = 5-6 membered aromatic or saturated (substituted) heterocyclyl, Ph], were prepared Thus, 1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxamidine (preparation given), 3-dimethylamino-2-methylsulfonyl-2-propenenitrile, piperidine, and isoamyl alc. were heated 12 h at 110° to give 31.8% 3-(4-amino-5-methylsulfonylpyrimidin-2-yl)-1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine. Tested I increased

cGMP levels by 600% to >1000%.

IT **256498-64-3P 256498-66-5P 256498-67-6P 256498-84-7P 256498-86-9P 256498-91-6P 256498-92-7P 256498-93-8P 256498-97-2P 256498-98-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzylpyrazolopyridines and related compds. as cardiovascular agents)

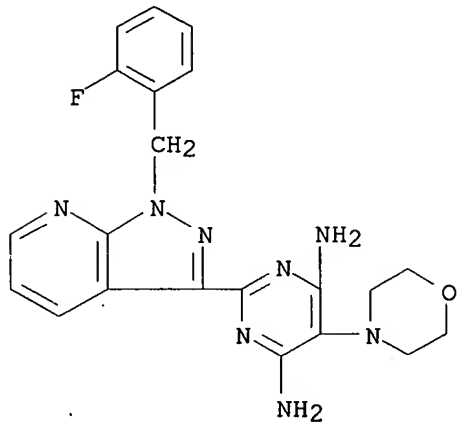
RN 256498-64-3 CAPLUS

CN 5-Pyrimidinecarbonitrile, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



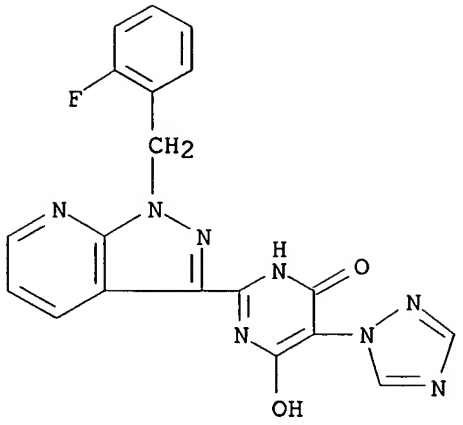
RN 256498-66-5 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-5-(4-morpholinyl)- (9CI) (CA INDEX NAME)

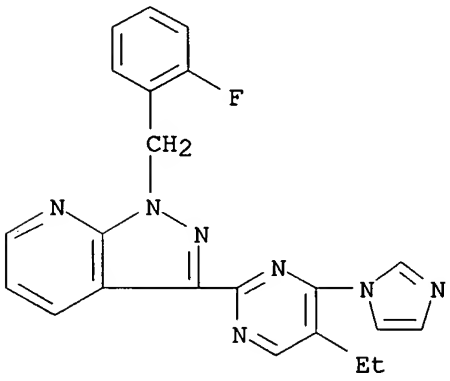


RN 256498-67-6 CAPLUS

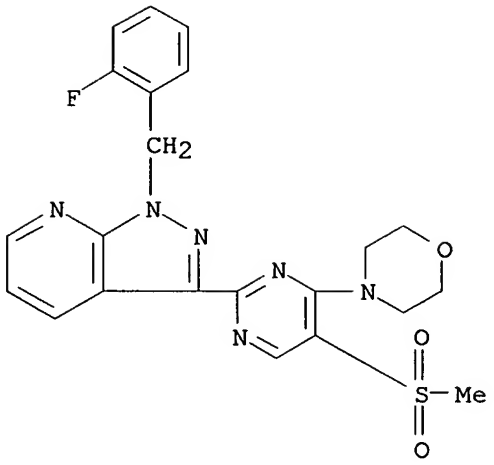
CN 4(1H)-Pyrimidinone, 2-[1-[(2-fluorophenyl)methyl]-1H-pyrazolo[3,4-b]pyridin-3-yl]-6-hydroxy-5-(1H-1,2,4-triazol-1-yl)- (9CI) (CA INDEX NAME)



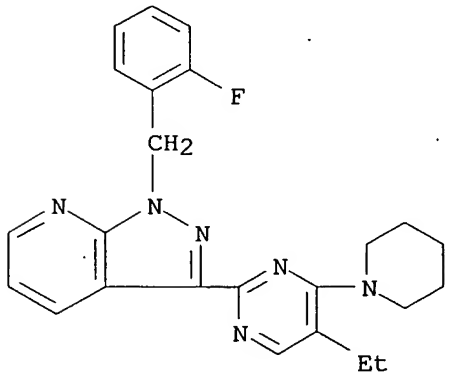
RN 256498-84-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-ethyl-4-(1H-imidazol-1-yl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



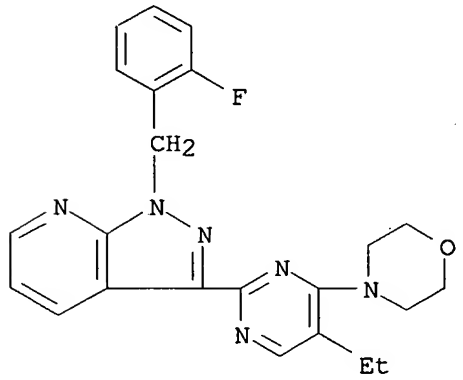
RN 256498-86-9 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 1-[(2-fluorophenyl)methyl]-3-[5-(methylsulfonyl)-4-(4-morpholinyl)-2-pyrimidinyl]- (9CI) (CA INDEX NAME)



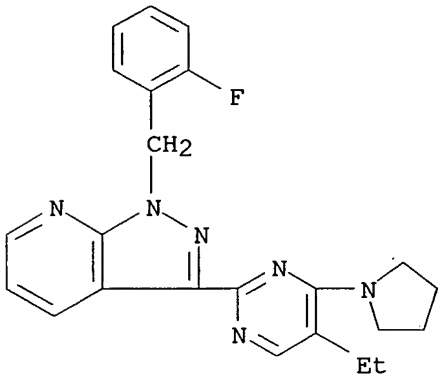
RN 256498-91-6 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-ethyl-4-(1-piperidinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



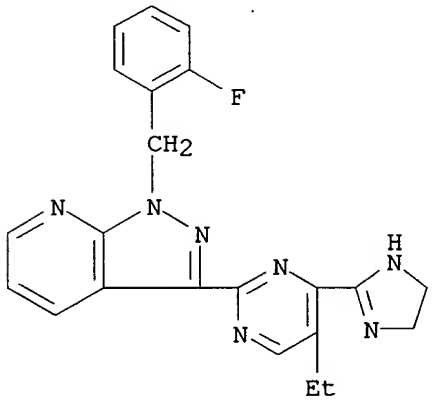
RN 256498-92-7 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-ethyl-4-(4-morpholinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



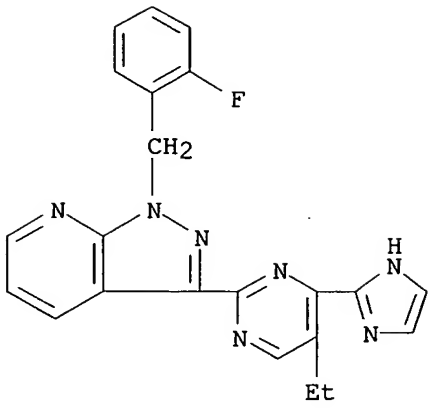
RN 256498-93-8 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-ethyl-4-(1-pyrrolidinyl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 256498-97-2 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[4-(4,5-dihydro-1H-imidazol-2-yl)-5-ethyl-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 256498-98-3 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine, 3-[5-ethyl-4-(1H-imidazol-2-yl)-2-pyrimidinyl]-1-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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